In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

No. 08-799V
Filed: June 20, 2012
Unpublished

REBECCA CROSBY, parent of ETHAN CROSBY, a minor,	*	Entitlement; Diphtheria, tetanus, acellular pertussis, DTaP; Transverse myelitis, TM; Althen prong III; Molecular mimicry; Timing of an adaptive immune response in a primed individual, anamnestic response; Time required for a measurable adaptive immune response versus time required for manifestation of clinical symptoms of an adaptive immune response; Medically-appropriate time for onset
Petitioner,	*	
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Ronald Craig Homer, Conway, Homer & Chin-Caplan, P.C., Boston, MA, for Petitioner.
Debra A. Filteau Begly, U.S. Department of Justice, Washington, D.C., for Respondent.

DECISION ON ENTITLEMENT[1]

GOLKIEWICZ, Special Master.

I. INTRODUCTION

Petitioner filed her Petition on behalf of her son on November 10, 2008, claiming entitlement to compensation under the Vaccine Act.[2] Petitioner claims her son suffered from a

[1] The undersigned intends to post this decision on the website for the United States Court of Federal Claims, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002). **As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire decision will be available to the public. Id. Any motion for redaction must be filed by no later than fourteen (14) days after filing date of this filing. Further, consistent with the statutory requirement, a motion for redaction must include a proposed redacted decision, order, ruling, etc.**

[2] This Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 et seq. (2006) (hereinafter "Program," "Vaccine Act," or "the Act"). Hereafter, individual section references will be to 42 U.S.C. §§ 300aa of the Act.

spinal cord injury, transverse myelitis,[3] with accompanying, persistent deficits as a result of the vaccinations he received on December 13, 2005. See Petitioner's Pre-Hearing Submission, filed Apr. 19, 2011. In support of her case, petitioner submitted expert opinions from Dr. James Renfroe and Dr. Vera Byers. Respondent filed her Rule 4(c) Report on April 13, 2009, recommending against compensation. Respondent relied upon the expert opinions of Dr. John Sladky and Dr. Noel Rose in support of this position.

Despite a great deal of expert medical evidence, the crux of the case is a factual question – when was the onset of Ethan's alleged injury. This is so because, as will be discussed in detail, the undersigned finds the alleged injury occurred within 24 hours of immunization. Twenty-four hours from vaccine to onset is a time period that all of the experts agree is too short to be medically appropriate for vaccine-relatedness. Regarding this factual issue, the experts disagree on the interpretation of the medical records and petitioner's affidavit. Respondent's expert neurologist finds the medical records, the parents' descriptions of neurological symptoms, and the timing of those symptoms to be wholly consistent with the clinical course of transverse myelitis unrelated to vaccination. Petitioner's experts, in contrast, make speculative and strained attempts to explain away the medical records and factual evidence to present a picture of timing that is appropriate for vaccine-causation. Both parties presented well-credentialed experts; however, the persuasiveness of the individual experts and their use of the underlying medical records were not equal. Ultimately, as discussed below, petitioner is unable to show preponderant evidence of a medically appropriate time frame and thus the vaccinations her son received on December 13, 2005, were not the cause of his spinal cord injury.

II. PROCEDURAL HISTORY

The Petition was filed on November 10, 2008. Petitioner's ("P") Petition for Vaccine Compensation ("Petition" or "Pet."), filed Nov. 10, 2008. Until February 11, 2009, petitioner collected medical records. See P Statement of Completion, filed Feb. 11, 2009. Respondent filed the Rule 4(c) Report on April 13, 2009. Respondent ("R") Rule 4(c) Report ("Report"), filed Apr. 13, 2009. As previously noted, respondent challenged entitlement to compensation under the Act, noting that treating physician records did not identify the vaccinations as causative and that petitioner had yet to submit a supportive medical opinion. R Report at 9. Petitioner filed her expert report from Dr. Renfroe, with accompanying medical literature, on August 17, 2009. P Ex 20, filed Aug. 17, 2009. Respondent thereafter filed the responsive report from Dr. Sladky on November 2, 2009. R Ex A, filed Nov. 2, 2009.

A hearing was scheduled for May 13, 2010, and medical literature and prehearing filings were submitted. Hearing Order, filed Jan. 8, 2010. On May 4, 2010, the undersigned issued an Order cancelling the May 13 Hearing at the parties' suggestion. Order, filed May 4, 2010. This occurred to allow petitioner the opportunity to seek an expert report from an immunologist. Id. Petitioner filed her expert report from Dr. Byers with additional medical literature on August 2, 2010. P Ex 31, filed Aug. 2, 2010. In response, respondent filed the expert report from Dr. Rose

[3] In the Petition, petitioner claimed Ethan suffered from flaccid paraplegia and spinal cord injury. Petition at 1, filed November 10, 2008. It will be discussed that there was some contention between the parties regarding the proper diagnosis of Ethan's injury.

on October 1, 2010. R Ex B, filed Oct. 1, 2010. Petitioner filed a supplemental report from Dr. Renfroe on January 26, 2011, P Ex 33, and a hearing was set for May 10 and 11, 2011. Additional exhibits were filed prior to this Hearing.

The Hearing occurred on May 10 and 11, 2011. Thereafter, the parties noted their preference for a schedule for filing post-Hearing briefs, which was accepted, and post-Hearing Briefs were filed. Joint Status Report, filed May 26, 2011; Scheduling Order, filed May 31, 2011; P Post Hearing Brief, filed Aug. 22, 2011; R Post Hearing Brief, filed Oct. 28, 2011; P Response to Respondent's Post Hearing Brief, filed Nov. 21, 2011. As such, this case is ripe for decision.

III. FACTUAL HISTORY

Petitioner's pregnancy with her son was relatively normal, only complicated by hypertension toward the end of the pregnancy; petitioner also had a diagnosis of a Factor V Leiden genetic mutation, which can lead to formation of blood clots. Pet. at 2; P Ex 16 at 1; P Ex 1 at 41; P Ex 4 at 48, 53, 55. Petitioner's son was born on August 13, 2005, by caesarean section. See, e.g., P Ex 3 at 25. He was given a vaccination for hepatitis B at birth. P Ex 4 at 1. He developed a slight case of jaundice that resolved before a pediatrician visit on August 23, 2005. P Ex 16 at 1; P Ex 4 at 53-54. Beyond this, Ethan was assessed to be a well child at his three day pediatrician visit, "perky, alert" at his ten day visit, and "thriving" at his two month pediatrician visit by Dr. Frostad. P Ex 4 at 53-54. At the two month visit, Ethan received the following vaccinations without apparent incident: diphtheria-tetanus-acellular pertussis ("DTaP"), haemophilus influenza type b ("Hib"), polio ("IPV"), and pneumococcal ("PCV"). P Ex 4 at 54. These were the same vaccinations Ethan received on December 13, 2005, and the reason the experts refer to Ethan as being "primed." Infra p. 8-9 (discussing the importance of the previous vaccination in terms of timing an adaptive immune response).

On December 13, 2005, Ethan was seen for his four-month check up. P Ex 4 at 44. During this visit, he received his second vaccinations of DTaP, Hib, PCF and IPV. Id. He was noted to be "well, no specific issues at all" and "thriving" at this visit. Id.

On the same day, December 13, petitioner described her son as being "very cranky" and that he "cried for several hours that night" following the pediatrician visit. P Ex 16 at 2. She noted he "finally fell asleep but had a very fitful night." Id. While breastfeeding, petitioner noted that "he was weaker, and had a harder time eating than previously before." Id. "The next morning his legs were like limp noodles, and he was unable to move them." Id. Ethan was noted to have a weak cry, was apathetic and had a slight temperature elevation. Id. Petitioner also described him having a poor appetite, difficulty swallowing and slept most of the day. Id. She noted these symptoms continued for several days and then "**slowly improved but he still could not move his legs and would stiffen if I tried to bend them**." Id. (emphasis added)

The observations found in petitioner's affidavit are confirmed in a contemporaneous history the parents created and provided to his pediatrician, presumably at the December 19 pediatric visit. Id. at 43. The relevant portions of the parents' written history read as follows:

> Tue: legs sore, baby fussy, slept poorly[;] Wed: limp noodle legs, couldn't cry . . . took long hot shower with him and vigorously pumped legs, no reaction. Apathetic[;] Thu: same behavior plus breathing became raspy . . . legs do not move at all, completely limp . . .[;] Fri: Baby is eating better . . . but still not near normal. Legs occasionally give a shiver when I try to stand him up. If I thump the bottom of his foot he will flinch the legs . . . [;] Sat: Seems good natured now . . . wiggles leg when I tickle it . . . [;] Sun: Moved legs slightly when asleep, 1st thing in morning legs scrunched up to belly[,] made diaper changing difficult . . . .

P Ex 4 at 43. There was discussion during the May 10 and 11 Hearing regarding when this history was created. Transcript of May 10-11, 2011 Hearing at 39-43 ("Hr'g Tr. at"). The pediatrician's note from December 17 states, "Mother and dad are to observe kid closely. . . . Dad to write down a log of this baby's behaviors every day since the illness started." P Ex 4 at 44. Then, the December 19 pediatrician visit referenced Ethan's history, noting "this is documented well by parents' history that they bring in." As was discussed during the Hearing, it is reasonable to assume that the parents' history included in the pediatric records was created at some point between December 17 and December 19. Hr'g Tr. at 42-43.

Ethan saw his pediatrician on December 17, 2005, with complaints of hypotonia and decreased use of his legs. P Ex 4 at 45. There is a note that he wiggled his legs that morning when tickled. Id. The pediatrician noted "motor tone decreased. Reflexes good . . . if I pinch his foot, he withdraws the leg away. He did not have any significant spontaneous movement at all of the lower extremities, would not support weight on his lower extremities at all, just still hanging, with very decreased motor tone." Id.[4]

Ethan was reevaluated on December 19, 2005. P Ex 4 at 44-45. His parents noted there were minimal spontaneous leg movements but some of Ethan's symptoms were improved. Id. at 44. Due to the presence of reflexes, Guillain-Barré Syndrome was ruled out. Id. at 45. A neurologist was consulted. Id. Included in the pediatric record is a parents' written history of their observations that was discussed previously. P Ex 4 at 43.

On December 20, 2005, a child neurologist, Dr. MacDonald, examined Ethan. P Ex 4 at 48-52. Upon initially seeing the neurologist, Ethan's parents filled out the Patient History Form, noting that Ethan had not "consciously moved his legs in a week after receiving 4 month vaccines." P Ex 8 at 52. In the neurologist's own review of the case following a phone call with

[4] As is discussed at different points in this Decision, petitioner called into question the accuracy of information found in the pediatrician's December 17 note and also questioned whether or not Ethan was even seen by the pediatrician on December 17 at all. P Post-Hearing Brief at 28, filed Aug. 22, 2011. The record notes that this entry was dictated on January 10, 2006, when it was brought to the doctor's attention that a chart entry was not created in association with a billing slip. P Ex 4 at 45. In support of the fact Ethan saw the pediatrician on December 17, the note describing the next pediatric encounter on December 19 notes that Ethan was seen on "**Saturday in the office, now comes back in today**." Id. at 44 (emphasis added). December 17, 2005, was a Saturday; December 19, 2005, was a Monday. There is no evidence or argument that the December 19 pediatric note was created after-the-fact. When the neurologist is consulted on December 19, a phone call occurred between the pediatrician and neurologist. P Ex 8 at 53. The neurologist's note about the phone call states, Ethan was "**seen Sat[urday**] – normal [deep tendon reflexes] and sensation, but decreased tone legs [greater than] arms." Id. (emphasis added). "**Seen this A.M**. – little [change], improved a bit." Id. (emphasis added).

Ethan's pediatrician, the neurologist noted Ethan was not using his legs after the vaccination and that he was "better by day 3." Id. at 53. There is no indication to what "better" refers. His note continued, "seen Sat[urday] – normal [deep tendon reflexes] and sensation, but decreased tone legs [greater than] arms." Id. "Seen this A.M. – little [change], improved a bit. Feeding ok, not sick." Id. "? ADEM or Transv[erse] myelitis? Doubt directly related to imm[unization]?" Id. This record indicates the treating neurologist actually discussed Ethan with the pediatrician on December 19, the day before the neurologist saw Ethan. P Ex 8 at 53 ("spoke with Dr. [] Frostad" . . . "Offered advice consult. – tomorrow . . . ").[5] He noted that there was no significant fever or local reaction following the vaccinations and that Ethan had not had adverse reactions to prior immunizations. Id. at 49. The history includes mention that "he woke after an unremarkable night's sleep[,] he was limp and could not move his lower extremities." Id. He reiterated the apathy and lethargy noted by the parents and pediatrician in the two to three days after immunizations. Id. The impression was:

> Ethan has experienced the relatively abrupt onset of diffuse weakness and hypotonia with preserved alertness. There has been some change in his demeanor, voice and feeding ability concomitant with this. This followed very closely on the heels of an uncomplicated four-month immunization. His examination is remarkable for hypotonic quadriparesis with brisk reflexes and upgoing toes affecting the legs more than the arms and neck. . . . Given the rapid evolution of these neurologic findings in a previously healthy child I would be highly suspicious of the possibility of an acute monophasic demyelinating disorder such as acute [dis]seminated encephalomyelitis [("ADEM")][6], an unusual presentation of central nervous system mass or infarct remain in the differential diagnosis. At this point he is slowly improving which would also be consistent with an acute demyelinating event. There is no evidence of any severe metabolic derangement, acute infection, intoxication or other systemic illness that could cause his difficulties.

P Ex 4 at 51-52. Ethan was admitted to the hospital for evaluation and treatment.

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[5] As noted previously, supra p. 4 n. 4, this entry, which contains the notes by the neurologist discussing Ethan's case with the pediatrician by phone on December 19, is consistent with the recollected notes on Ethan's December 17 pediatrician visit. Compare P Ex 4 at 45; with P Ex 8 at 53. This conversation occurred closer in time to the December 17 visit than January 10, 2006, the date the exam note was created. As discussed, the notes of the December 17 visit were called into question by petitioner in particular because they were not dictated on the day of the visit.

[6] Acute disseminated encephalomyelitis or ADEM is:

> An acute or subacute encephalomyelitis or myelitis characterized by perivascular lymphocyte and mononuclear cell infiltration and demyelination; it occurs most commonly following an acute viral infection, especially measles, but may occur without a recognizable antecedent. It formerly occurred as a complication of rabies vaccination before the introduction of duck embryo and human diploid vaccines and of smallpox vaccination. It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system. Clinical manifestations include fever, headache, vomiting, and drowsiness progressing to lethargy and coma; tremors, seizures, and paralysis may also occur; . . . many survivors have residual neurologic deficits.

DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 621 (31st ed. 2007).

During his nine-day hospital stay, he underwent MRIs, a lumbar puncture, three days of high-dose steroids, five days of intravenous immunoglobulin, an electrocardiogram and physical therapy and occupational therapy consultation. P Ex 4 at 46. Ethan's neuroimaging studies were normal and the spinal fluid analysis revealed non-inflammatory spinal fluid. Id. The discharge diagnosis was "1. Myelopathy secondary to acute disseminated encephalomyelitis (demyelinating disorder). 2. Lower extremity weakness and hypotonia. 3. Bradycardia due to intravascular volume expansion." P Ex 4 at 46-47. It was noted that his condition was stable but continued to have significant weakness. The discharge summary further discusses possible causes:

> A number of other etiologies for the patient's complaint were entertained during the time of his hospital stay. There was no evidence of systemic vasculitis, inflammation, or infection. There was no evidence of a spinal or dural vascular malformation on his spinal MRI and no evidence of any bony impingement on the cord. The response to intravenous immunoglobulin and steroid treatment may be delayed for as much as 2 weeks following completion of the treatment course. His prognosis at this point is cautiously optimistic for continued improvement in lower extremity strength and function. There is certainly a possibility for permanent neurologic deficit following this demyelinating episode.

P Ex 4 at 47. Vaccinations were not mentioned as a possible cause of Ethan's condition at discharge. Ethan's parents were given instructions to follow up with Dr. MacDonald. Id. at 46. Petitioner reported that "[a]bout a month after he came home, his legs started to twitch occasionally." P Ex 16 at 3.

Physical therapy was started on January 1, 2006, with a stated diagnosis of transverse myelitis ("TM"),[7] noting that "the causal agent has still not been discovered." P Ex 9 at 105. He saw Dr. MacDonald again on January 11, 2006. P Ex 4 at 34-35. Ethan was slightly improved with "his upper extremities, trunk, neck and head functioning normally." Id. at 35. Ethan could "bear a slight amount of weight in his lower extremities when supported in a standing position. This represents an improvement from his nadir." Id. Dr. MacDonald noted that he "remains at risk of functional immunosuppression for about six months following his high dose steroid treatment . . . . I would recommend that he not have any immunizations for at least the next six months while we wait for him to recover." Id. At Hearing, respondent's expert neurologist explained that Ethan's vaccinations were held immediately following his injury because of his immune-compromising treatment with immunoglobulin and steroids. Hr'g Tr. at 152.

Ethan saw his pediatrician, Dr. Frostad, on February 10, 2006. It was noted that there was "no definitive diagnosis" but they were "still considering transverse myelitis." P Ex 4 at 21.

[7] Transverse myelitis, or TM, is "an acute demyelinating disorder of the spinal cord that evolves in hours or days." P Ex 20 at 3 (citing P Ex 20-A, Gerald M. Fenichel, CLINICAL PEDIATRIC NEUROLOGY 264-65 (5th ed. 2005)). "As in adults, acute transverse myelitis in children appears to be a self- and time-limited illness and is generally monophasic. Improvement generally occurs two to 12 weeks after maximal deficit." P Ex 20-C, RMS Riel-Romero, Acute transverse myelitis in a 7-month-old boy after diphtheria-tetanus-pertussis immunization, 44 SPINAL CORD 688 (2006). "Transverse myelitis is a focal inflammatory process involving the spine that is thought due to some type of autoimmune response. Autoimmune meaning that the child's myelin, or whatever is being attacked, is perceived as being foreign so the body attacks it." Hr'g Tr. at 10.

The pediatrician noted that the neurologist recommended postponing vaccinations for six months. Id. A visit to Dr. MacDonald on February 21, 2006, showed continued improvement. P Ex 8 at 94-95; P Ex 4 at 31. Dr. MacDonald saw Ethan again on April 20, 2006, at which time the parents inquired about Ethan returning to day care and his subsequent immunizations. P Ex 8 at 100-01; P Ex 4 at 27. Dr. MacDonald noted Ethan's prior vaccinations and that he should have "reasonable immunity" to return to day care. P Ex 8 at 101. The doctor notes the parents' reluctance to continuing vaccinations but that he had no "specific neurologic contraindication" to further vaccinations and suggested the parents consult Ethan's pediatrician. Id. "Certainly, the functional immunosuppression from his high dose steroid treatment should be gone by the time he is 10 or 12 months old, and immunizations would thereafter be expected to be efficacious." Id. "His parents are worried about possible recrudescence of a demyelinating problem with the immunizations. I reassured them that this is a low risk but understand their trepidation." Id. at 100. Dr. MacDonald again noted in July 2006 that "it is reasonable to resume his immunizations." P Ex 8 at 106.

On August 9, 2006, Ethan was seen by his pediatrician for a one-year well check. P Ex 4 at 22. Ethan was noted to be "doing well considering he had a bout of transverse myelitis, requiring hospitalization." Id. Gross motor delays continued. Id. Immunizations were also discussed.

> We reviewed his immunizations, which he is definitely behind on – parents hesitant to restart immunizations, given the timing of his transverse myelitis being a few days after his immunizations at 4 months. **Mom understands the neurologist feels the two events were not related, other than just in time – he recommends continuing his immunization series.** Mom says dad is willing to proceed with immunizations, but mom herself is not quite ready yet. . . . Will see him at 15 months for a well check, or sooner if mom is willing to restart his immunizations series.

P Ex 4 at 19 (emphasis added).

On August 16, 2007, Ethan was seen by Dr. Dunbrasky, who noted he was not current on vaccinations. "Mom has some concerns with [TM] being associated with his immunizations due to the timing. **He had received his shots the day before. The following day Mom noted he could not move and he was hospitalized**." P Ex 12 at 1 (emphasis added). There appears to be no indication in the medical records that any of Ethan's treating physicians identified his immunizations as causative of his injury. Dr. Renfroe, petitioner's expert neurologist, agreed that no treating doctors commented on vaccine causality. Hr'g Tr. at 20.

Records and petitioner's affidavit indicate that Ethan continues to suffer motor problems, takes medication for spasticity in his legs, wears braces to walk and stand, knee immobilizers at night, has a diminished sense of pain in his legs and continues to participate in therapy. See, e.g., P Ex 16. At the time petitioner's affidavit was created, Ethan still suffered from residual complications of his TM and standing and walking on his own were problematic. Id. He began physical therapy following the initial hospitalization and this is ongoing to this day. P Ex 16 at 2.

IV. EXPERT EVIDENCE

The undersigned notes that four well-qualified experts, two neurologists and two immunologists, testified for the parties in this case. This case was not a typical battle of the experts; there was much upon which the experts agreed. Where there were differences in the opinions and interpretation of the medical records, the undersigned found respondent's experts better qualified and more persuasive.

Before discussing the experts' opinions and testimony, the undersigned points out a critical distinction of which a reader must be aware. The experts discuss two concepts: a) an adaptive immune response or an autoimmune response that is evident at first only by measurement of antibodies in a patient and b) the development of symptoms of an injury caused by that autoimmune or adaptive immune response, signs that actual damage is occurring in a patient. The former would be measured by antibodies circulating in a person's system. The latter would be the symptoms, such as the inability to use one's legs with TM, that a person experiences or observes. It was stressed that these are two phases separated by some amount of time when discussing an injury caused by an autoimmune process. One must first develop the immune response before one sees the symptoms of injury from that response. In order for the symptoms of the autoimmune injury to manifest, the autoimmune or adaptive immune response must have developed, proliferated, traveled to the site of injury and had sufficient time to cause enough damage that the injury manifests symptoms. See infra pp. 23-26, 44-45. The undersigned found that the experts' references to these two stages, particularly the references by petitioner's experts, to be confusing and lax in regard to which process they referred throughout the Hearing.

Another important concept should also be noted as it is discussed throughout. In their reports and testimony, the experts referenced Ethan as being primed,[8] or having a secondary or anamnestic[9] response to the vaccinations received on December 13, 2005. These terms refer to the fact that Ethan was exposed to these vaccines two months prior and thus, the December 13 vaccine components were encountered by his immune system previously. If the prior vaccinations worked properly, Ethan would have an immunologic memory of an adaptive immune response[10] to those antigens. The concept of an individual being "primed" is important regarding what the appropriate amount of time between vaccination and onset of TM would be – Althen prong three. There is no dispute that Ethan received the same vaccines approximately

[8] "Immunologically activated by initial exposure to antigen; said of cells of the immune system." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1537 (31st ed. 2007).

[9] Anamnesis means "immunologic memory." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 74 (31st ed. 2007).

[10] It is discussed throughout, but for clarity reasons the undersigned notes our immune system is comprised of two general types of responses. The first, the innate response, is what all people are born with and makes up the "first line of defense" to antigens. This response is not specific to the particular antigen but is meant to engulf invaders and secrete chemicals to communicate the encounter, which recruits other cells to the site of injury or infection. This innate response also begins the adaptive response. The adaptive response is the system by which our bodies develop a more tailored response to the antigens we encounter. It attempts to remedy any threats that survive past the innate response and creates a memory of sorts to respond to the antigen if it is encountered a subsequent time. See P Ex 31 at 3-5; R Ex B at 3-4.

two months prior and the experts do not dispute the fact that the adaptive immune response in a primed individual would occur faster than the adaptive response in an individual who is encountering the antigen for the first time. See, e.g., P Ex 31 at 5 (noting Ethan's "immune system has been 'primed' by earlier vaccines"); R Ex B at 4 (noting that an adaptive immune response takes one to two weeks after a primary exposure to develop, whereas a secondary exposure to an antigen takes at least ninety-six hours).

A. Expert Reports

Petitioner submitted her first expert report, by Dr. Renfroe, on August 17, 2009. Dr. Renfroe's opinion, his CV and accompanying medical literature were submitted on August 17, 2009. Dr. Renfroe is a pediatric neurologist and is board certified by the American Board of Psychiatry and Neurology with special training in the care of children. P Ex 21; Hr'g Tr. at 5-6, filed Jun. 21, 2011. Dr. Renfroe testified to seeing ten to twenty cases of transverse myelitis in his career. Hr'g Tr. at 7.

In his opinion, Dr. Renfroe describes the relatively uneventful time leading up to Ethan's TM, P Ex 20 at 1-2, and the events surrounding the vaccinations and onset of TM. Id. at 2. Dr. Renfroe's review of the facts mirrors those described above, particularly that the parents note onset of weakness within 24 hours of vaccination. P Ex 20 at 3.[11] He believes the child's symptoms and findings are consistent with TM. P Ex 20 at 3. He notes that the family reported onset within 24 hours after immunization but "medical evaluation was delayed until 4-6 days after the immunizations." Id. He continues by stating TM "'often occurs when your body's immune system mistakenly attacks its own tissues, resulting in inflammation and injury to the fatty insulating material that covers nerve cell fibers (myelin) within your spinal cord.'" P Ex 20 at 3 (citing P Ex 20-B, MayoClinic.com, Transverse Myelitis website). It appears that Dr. Renfroe offers an autoimmune reaction to the vaccination as the theory of causation. This report contains no discussion of what is a medically appropriate time frame between vaccination and onset of the condition.

Dr. Renfroe states that both the DTaP and the hepatitis B vaccines have been **associated with** TM. P Ex 20 at 3 (emphasis added). For this proposition, Dr. Renfroe cites a 2006 case report discussing a 7-month-old boy having TM following a DTaP immunization, which was given 17 days prior to the child's hospitalization. P Ex 20-C, RMS Riel-Romero, Acute transverse myelitis in a 7-month-old boy after diphtheria-tetanus-pertussis immunization, 44 SPINAL CORD 688 (2006). The author notes, "[i]t is possible that our patient had a postinfectious or a postvaccination acute transverse myelitis as his symptoms occurred about 2 weeks after an upper respiratory infection and 17 days after a DTaP vaccination." P Ex 20-C at 3. The article discusses other reports of TM following vaccination: 6-month-old baby with flaccid quadriparesis 17 days after a DTP vaccination; 7-month-old who developed flaccid paraplegia 6 days after immunization with DT and oral polio; 15-month-old child with acute TM 21 days after

[11] Dr. Renfroe notes that the December 17, 2005 exam note was dictated from memory approximately three weeks following the actual visit. P Ex 20; see also P Ex 4 at 44-45. It is again noted that the pediatrician's note on December 19 and the note of the pediatrician's phone call to the neurologist on December 19 provide some level of corroboration to the recollected December 17 exam note. See P Ex 4 at 44-45; P Ex 8 at 53.

an MMR vaccination; a 15-year-old girl with right-sided weakness and numbness 1 week after hepatitis B vaccination; a 4-year-old girl with TM 14 days after the Japanese B encephalitis vaccination; a 9-year-old girl with TM 16 days after measles and rubella vaccination. Id. The report notes cases concerning adults as well. Id. The author of the article discusses molecular mimicry as the mechanism by which the body's own immune system attacks the spinal tissue. Id. The author states, "[i]n our patient, we were not able to discover an associated agent despite an extensive diagnostic work-up. **The history of fever and upper respiratory symptoms 2 weeks before the onset of the symptoms suggests a viral agent**." Id. (emphasis added). Retrospective analysis of 33 reported cases shows that 46% of the patients had a preceding infection. Id. Vaccination and preceding infections both appear to suggest the possibility of an autoimmune process at work. Id. However, the author states, **"[a]lthough there is a temporal relationship between the development of transverse myelitis and DTaP vaccination in our patient, it is difficult to establish a causal relationship between the two. The occurrence could have been simply coincidental**." P Ex 20-C at 3 (emphasis added).

On November 2, 2009, respondent responded by filing an expert report from Dr. Sladky. R Ex A, Report of Dr. John Sladky; R Ex A-1, CV of John Thomas Sladky, M.D. Dr. Sladky is also a pediatric neurologist and board certified by the American Board of Pediatrics, the American Board of Psychiatry and Neurology with Special Competence in Child Neurology, and the American Board of Electrodiagnostic Medicine. R Ex A-1.

Dr. Sladky's opinion, like that of Dr. Renfroe, begins with a recitation of the facts consistent with what was previously discussed. R Ex A at 1-2. Dr. Sladky notes that "Ethan has had several subsequent MRI scans all of which have been normal. Consequently, his diagnosis of 'acute demyelinating disease,' something falling under the acute disseminated encephalomyelitis/transverse myelitis rubric, remains presumptive." Id. at 2. In fact, in Dr. Sladky's opinion, "[t]he nexus of this case is the complete absence of any corroboratory data reinforcing the notion that this child suffered an autoimmune mediated, inflammatory injury to the spinal cord which could have been triggered by an inciting immunological challenge such as a vaccine or infection." Id. He points out that all tests were normal and "there are no clinical features which suggest a specific etiology for this child's myelopathy." Id.[12]

[12] Other alternative etiologies for Ethan's condition are speculated, particularly spinal cord infarction or stroke. R Ex A at 3. Looking at the clinical data from Ethan's December 17 and December 20 examinations, Dr. Sladky notes "the meager clinical information does not substantially favor one diagnosis over the other." R Ex A at 3. Discussing the spinal fluid examination, "the absence of evidence of inflammation in the spinal fluid would be expected in the case of a small infarction in the spinal cord but viewed as more exceptional in the context of autoimmune demyelinating disease." Id. Further, Ethan's normal MRIs are unexpected in an acute demyelinating event. Id. Dr. Sladky also notes petitioner's own Factor V Leiden gene mutation, which apparently Ethan was not tested for when Dr. Sladky's report was filed. Id. The mutation, which Ethan had a 50% chance of inheriting, "confers as increased risk of formation of blood clots in childhood leading to stroke." Id. "[E]ven ignoring the issue of a possible underlying coagulation disorder, a strong argument can be made that stroke is a more likely cause for Ethan's neurological injury than autoimmune disease. If Ethan carries the Leiden mutation it becomes even more persuasive." Id. Ultimately, Dr. Sladky finds the possibility of a spinal cord stroke was "ignored despite the recognition that his mother is known to carry the Factor V Leiden mutation which confers increased risk for this complication." R Ex A at 4. Because the undersigned finds preponderant evidence in petitioner's favor that Ethan suffered from TM, this evidence is not discussed at length. See infra p. 30-31.

Dr. Sladky agrees with Dr. Renfroe that the normal diagnostics do not rule out TM as a possible diagnosis. "Because they do not contribute positive diagnostic information, however, does not imply that they are without weight and can be eliminated from the calculus." Id. Regarding causation, Dr. Sladky looks at three "postulates" to support petitioner's theory: "1) [T]hat the vaccine in question is a known cause of the neurological complication; 2) that the clinical features are consonant with those which would be anticipated from the recognized biology of the disease; and 3) that there is tangible evidence that immunization instigated the autoimmune process resulting in neurological injury." R Ex A at 3-4.

Regarding evidence that the vaccine here can cause such an injury, Dr. Sladky notes that case reports are anecdotal evidence that do "not rise to that level of credibility and fail to substantiate the contention" that the vaccine was the cause. R Ex A at 4.

In the context specifically of Ethan's case, Dr. Sladky focuses on the very short time frame in which observable symptoms arose, within approximately 24 hours. Id. "In my view, this is an implausibly short time period to permit the complex cascade of immunological events necessary to effect tissue injury manifesting as motor paralysis." Id. He discusses review of this issue by the Institute of Medicine ("IOM") and animal models that have been used to study demyelinating disorders. "In general, the earliest clinical evidence of neurological dysfunction in these animal models emerges around seven days, with the majority in the range of ten to fourteen days."[13] According to Dr. Sladky, the IOM considered these observations important "in determining the range of conceivable latencies between immune challenge and the onset of disease." Id. After considering such evidence, "the IOM concludes that the latency between vaccination and the first symptom of illness should fall between 5 and 42 days to be considered credible." Id.; R Ex A-5 at 4, Institute of Medicine, ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINE, EVIDENCE BEARING ON CAUSALITY, 45 (1994)("a conservative estimate of the limits of the latencies . . . is considered to be from 5 days to 6 weeks"). Dr. Sladky goes further to opine that "[m]y own view is that these limitations are broader than actuality, however, I suspect that they are intended to provide considerable laterality for petitioners to make their case." Id. "In this instance, the duration between vaccination and the evolution of paralysis is far too brief to sustain an argument for a causal relationship." R Ex A at 4.

Regarding petitioner's contention that no other plausible causative agents were found, Dr. Sladky states, "[a]s is well known, despite arduous inquiry, no history of an antecedent event or infection can be elicited in roughly one third to one half of patients who contract transverse myelitis." Id. "[E]ven the time frame argues for coincidence rather than causality." Id. Medical literature in support of Dr. Sladky's report was filed on April 23, 2010.

Petitioner filed the expert report of Dr. Byers on August 2, 2010, with supporting literature. P Ex 31, Report of Dr. Vera Byers; P Ex 31 A-G, medical literature; P Ex 32, CV of Dr. Vera Byers. Dr. Byers describes herself as an internist and basic and clinical immunologist. P Ex 32 at 1. She is board certified by the American Board of Internal Medicine and has a Ph.D. in immunology. Id. Her report was filed as a supplement to the report of Dr. Renfroe. P Ex 31

[13] As was noted and will be discussed throughout, the distinction between when a person develops an autoimmune response and when a person develops symptoms of an injury caused by the autoimmune response is critical to understanding cases involving allegations of vaccinations causing demyelinating events. Supra p. 8-9.

at 1. She relies upon Dr. Renfroe for the diagnosis of TM and for the association between the vaccines Ethan received and TM. Id. "I was asked to discuss the events which occurred between the time the 12/13/05 vaccine was given and the onset of the disease, and the etiology of TM." Id. "The purpose of this report is to point out that the physical signs and symptoms that Ethan displayed during the first 3-4 days of his illness were non-specific and most likely due to his innate immune systems activation by the vaccines." Id.

Dr. Byers' report begins by examining the complaints in the first few days that followed Ethan's vaccinations. Interestingly, Dr. Byers characterizes the lower extremity problems only as "weak legs which continued for several days then improved." R Ex 31 at 1. There is no reference to where Dr. Byers gathers this description of these events or why she characterizes "no spontaneous movement" as simply "weak legs." She references the pediatrician's exam as finding from the December 17 visit as "decreased spontaneous movement of his legs." Id. Dr. Byers does not acknowledge the rest of the pediatrician's observations, those being "[h]e did not have any significant spontaneous movement at all of the lower extremities, would not support weight on his lower extremities at all, just still hanging, with very decreased motor tone." P Ex 4 at 45. Like Dr. Renfroe, Dr. Byers notes that this entry was made from the pediatrician's memory, approximately three weeks after the visit. P Ex 31 at 1. Dr. Byers also does not acknowledge petitioner's Affidavit, P Ex 16, which contends Ethan's condition improved, except for his leg symptoms.

Dr. Byers' impression of the December 19 pediatrician visit was that some symptoms had improved but Ethan's "[deep tendon reflexes] were 1+ in both upper and lower extremities, and now the motor weakness was localizing to the legs." P Ex 31 at 1. Dr. Byers stresses that "[t]he point to make is that **all the symptoms** reported in the immediate post-vaccine period were those that are expected to be produced by the interaction of the innate immune system with vaccines. They are nonspecific, and are more consistent with an encephalopathy than a localized spinal cord lesion." Id. at 2 (emphasis added). Dr. Byers does not explain how lack of movement in lower extremities is a sign of an encephalopathy and this issue was discussed at the Hearing. She opines that "it was only later, about 4-7 days after the vaccination that these nonspecific events begin to resolve, and the focal lesion associated with TM began to emerge." Id. By her own testimony, Dr. Byers is not a neurologist and her support for pinpointing onset of Ethan's TM four to seven days after vaccination was not discussed. Notably, the report from Dr. Renfroe available at this time does not specifically assert when Ethan's TM began. R Ex 20.

The undersigned notes that Dr. Byers' characterization of the facts and dismissal of the leg symptoms appear to be inconsistent with the medical records, the parents' hand-written history found in the pediatric records, the parents' histories in medical records recorded by medical personnel, and with the reports of Drs. Renfroe and Sladky. At the time when Dr. Byers' report was filed, there was no allegation that Ethan suffered an encephalopathy by the expert neurologists and no such report is found in his medical records.[14]

[14] See Hurd v. Sec'y of the Dept. of Health & Human Servs., No. 08-56V, slip op., 2010 WL 2022923, *6 (Fed. Cl. Spec. Mstr. Jul. 14, 2010)(noting an expert opinion may be rejected when an expert "assume[s] facts that are not supported by a preponderance of the evidence)(citing Brooke Group Ltd. v. Brown & Williamson Tobacco Corp., 509 U.S. 209, 242 (1993); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1376 n. 6 (Fed.Cir.1994).

Regarding the events during the first few days following Ethan's vaccinations, Dr. Byers alleges the innate immune system, the "first responder" of our immune systems, was responsible for the complaints Ethan's parents had and the findings upon examination by the pediatrician on December 17, 2005. She notes that common events occurring within the first seventy-two hours after vaccination with DTaP include: tenderness, erythema, induration, fever ≥ 38º, drowsiness, fretfulness, and vomiting; "There is also decreased appetite, prolonged high-pitched crying and more rarely high fever and seizures." R Ex 31 at 2 (citing 1998 Physicians' Desk Reference). A study of the VAERS database showed fever, irritability, drowsiness, restless sleep, and decreased appetite following the pneumococcal 7-valent vaccines. Id. (citing P Ex 31-F, Wise, et al., Postlicensure Safety Surveillance for 7-Valent Pneumococcal Conjugate Vaccine, 292 JAMA 14 (Oct. 2004)).[15] Dr. Byers points out that these were the symptoms noted by Ethan's parents in the days directly following vaccination. Regarding Ethan, the undersigned notes that there were no reports of injection site tenderness, erythema, induration, vomiting, high fever or seizure.

Dr. Byers' report goes on to discuss reports of ataxia,[16] gait disturbances, convulsions, meningitis and encephalopathy following the pneumococcal 7-valent vaccine and notes these reports are similar to the neurologic problem Ethan faced. P Ex 31 at 2.[17] Again, Dr. Byers is not a neurologist and up to this point in the case, no expert neurologist or treating doctor found ataxia, gait disturbances, convulsions, meningitis or encephalopathy.

It is unclear what is the basis for the assertion but Dr. Byers notes, "[m]ost of the reported events were simply caused by activation of the innate immune system and every one of those other vaccines [Ethan] received would have activated that same system." P Ex 31 at 2. As pointed out by Dr. Byers, all vaccines activate the innate immune system. Id. Dr. Byers then presents a general overview of the innate immune system's response, proinflammatory cytokines and autoimmune diseases. Id. at 2-5.

Ultimately, Dr. Byers' opinion is that the symptoms seen "between the time of the vaccination and the beginning diagnosis of ADEM/TM are completely consistent with those produced by proinflammatory cytokines synthesized and released by the innate immune system

[15] The authors' stated purpose of this article was "[t]o summarize reports of events occurring after vaccination with 7-valent pneumococcal conjugate vaccine (PCV), including those that may warrant further investigation to assess possible causation by PCV." P Ex 31-F. "**Because of important limitations in passive surveillance, data from VAERS require cautious interpretation.**" Id. (emphasis added). "VAERS is a database that compiles the reporting of any reaction to any immunization. Much of the reporting is voluntary, as only health care providers must report adverse reactions to vaccines listed on the Vaccine Injury Table." Manville v. Sec'y of the Dept. of Health & Human Servs., 63 Fed. Cl. 482 (Fed. Cl. 2004). Dr. Byers testified during the Hearing that VAERS is a passive reporting system and even a layman can submit a VAERS report and the system is set up to note trends but not show causation. Hr'g Tr. at 102-04.

[16] Ataxia is "failure of muscular coordination; irregularity of muscular action." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 172 (31st ed. 2007).

[17] The undersigned notes that the Wise article, P Ex 31-F, shows 49 reported cases of hypotonia following the PCV vaccination, which were not discussed by Dr. Byers. P Ex 31 at 3. The reports of hypotonia in this article, a symptom found in Ethan, were not examined beyond the bare number of VAERS reports; there is no information on when hypotonia began in those cases. Id.

in response to the vaccination." P Ex 31 at 5. In her view, the observable symptoms of Ethan's TM "probably began between 4-7 days after the vaccination." Id. The undersigned again notes that Dr. Byers is not a neurologist and she relied upon Dr. Renfroe for the opinion regarding the onset of Ethan's TM. Hr'g Tr. at 109-10. Her support for her opinion is a discussion of reported reactions in the VAERS database following the pneumococcal 7-valent vaccination. P Ex 31 at 5.[18] Thus, since Ethan was previously vaccinated with these vaccines, his system was already "primed" and this would lead to the cross reactivity or autoimmune reaction that resulted in his TM. Id.

Alternatively, "if Ethan had a dysregulated innate immune system, as is suggested by his strong clinical response to the vaccination, this could provide another mechanism by which the TM was initiated." P Ex 31 t 5. The undersigned is uncertain how this final, alternative theory is supported and there is no evidence in the medical records that Ethan suffered from a dysregulated immune system. In fact, as discussed above, Ethan was noted to be well and thriving prior to the onset of his TM, with no abnormal responses to past vaccinations or infections. Supra p. 3.

In response, respondent filed an expert report from Dr. Rose. R Ex B, filed Oct. 1, 2010. Dr. Rose is an immunologist and board certified by the American Board of Medical Microbiology, the American Board of Pathology, and the American Board of Medical Laboratory Immunology; Dr. Rose also has a Ph.D. in medical microbiology. R Ex B-1, CV of Dr. Noel Rose, filed Oct. 1, 2010. The undersigned was highly impressed with Dr. Rose's credentials, experience and the candor with which he testified at the Hearing.

Dr. Rose notes that the diagnostics performed on Ethan during his December 2005 hospitalization helped to rule out infarction, CNS tumor and multiple sclerosis. R Ex B at 2. He also notes the Fenichel text relied upon by Dr. Renfroe actually works against petitioner's case, as it states, "[t]he belief is widely held by many specialists that a prior infectious illness or immunization causes transverse myelitis, especially encephalomyelitis in children. **No evidence supports this belief**." R Ex B at 2 (quoting P Ex 20-A at 3)(emphasis added).

Dr. Rose's opinion primarily focuses on the opinion of Dr. Byers. He asserts that "Dr. Byers proposes that ADEM appeared in Ethan less than twenty-four hours after his second exposure to the vaccines and resulted in demyelination of the central nervous system . . . due to rapid production of early inflammatory mediators," which later developed into TM due to T lymphocytes cross-reacting with Ethan's own body. R Ex B at 3. Dr. Byers clarified during her Hearing testimony that Dr. Rose had misunderstood her report in that she never gave the opinion Ethan was suffering from ADEM that progressed into TM. Hr'g Tr. at 92-93.

Following a review of Dr. Byers' opinion, Dr. Rose discussed the innate and adaptive immune responses. Notably, the adaptive immune response requires days or weeks but can be "hastened if the host has previously encountered the same agent (i.e. been 'primed')." R Ex B at 4. However, initiation of the adaptive immune response still requires at least 96 hours. Id. This

[18] She goes on to say that TM is a "T cell disease," which is part of the adaptive immune response, and that it is therefore not possible to identify which vaccine or vaccine component specifically caused Ethan's condition. P Ex 31 at 5.

rapid secondary response is evidence of immunologic memory." Id. (citing R Ex B-6, Janeway, et al., Immunobiology: The Immune System in Health and Disease (6th ed. 2005)). He noted that the innate immune response, which Dr. Byers opined was the cause of the first few days of symptoms Ethan suffered, is tightly controlled. R Ex B at 4. The efficacy of vaccines hinges on their ability to avoid triggering an exaggerated innate immune response. Id. Dr. Rose explained that strict control over the innate immune response "explains the relative rarity of the autoinflammatory diseases in the general population and suggests that a combination of a genetic mutation with a powerful stimulus is required" to induce autoinflammation. Id. "The fact that Ethan did not have an adverse response to infections and has previously received vaccines with no problems suggests further that he has no inherited genetic impairment in controlling innate immunity." Id.

He explained that an adaptive autoimmune response usually "takes one or two weeks or more after first exposure to the antigenic trigger" and "at least four days" in an individual who is previously primed. R Ex B at 4. Thus, the time between vaccination and onset in Ethan "is much too rapid to suggest that the vaccinations could give rise to an adaptive immune response to cause" TM. Id. In general, Dr. Rose finds the opinions of petitioner's experts flawed:

> Dr. Renfroe proposes that the administration of the vaccines were directly responsible for the induction of [TM] based on literature citations of a co-occurrence of vaccination with the genesis of TM and the absence of any other defined cause. He fails to recognize that the association of vaccination with TM is based entirely on case reports and that there is no sound epidemiologic evidence establishing a statistically valid association. He also fails to provide a plausible biological mechanism whereby the vaccines can initiate the pathogenic process leading to TM within a period of less than 24 hours. Dr. Byers attributes the rapid onset of disease to the innate immune response. There is no foundation in our current understanding of the innate immune system to propose that it is the cause of a sudden monophasic, transient encephalopathy like ADEM and there is no known mechanism to account for the onset of TM within 24 hours after exposure.

R Ex B at 5.

Medical literature and a supplemental report from petitioner's expert, Dr. Renfroe, were filed on January 26, 2011. Dr. Renfroe discussed studies evaluating the time for an autoimmune response, noting that "most studies do not attempt to document an immune response prior to 3-5 days." P Ex 33 at 1 (citing P Ex 33-B, F.L. Gordon, et al., Rapid Entry and Downregulation of T Cells in the Central Nervous System During the Reinduction of Experimental Autoimmune Encephalomyelitis, 112 (1-2) J NEUROIMMUNOLOGY 15 (2001); P Ex 33-C, Robert S. Griffin, et al., Complement Induction in Spinal Cord Microglia Results in Anaphylotoxin C5a-Mediated Pain Hypersensitivity, 27(32) J NEUROSCI 8699 (2007)). Citing petitioner's Exhibit 33-D, Dr. Renfroe notes that "tagged T-cells in the CSF," which are evidence of an adaptive immune response, were noted 18 hours after an immune challenge. P Ex 33 (citing P Ex 33-D, David A Hafler & Howard L. Weiner, T Cells in Multiple Sclerosis and Inflammatory Central Nervous System Disease, 100 IMMUNOL REV 307 (1987)). Dr. Renfroe does not say whether the presence

of such cells would actually present with clinically observable symptoms within that time frame as well. He discusses petitioner's assertions of "priming," noting that priming can result in a "more robust response to subsequent antigenic challenge." P Ex 33 at 2. He also discussed a piece of medical literature addressing the "complex mechanism of the immune response in the CNS and how it can be augmented by exposure to certain pathogens." Id. (citing P Ex 33-E, Steven M. Kerfoot, et al., TLR4 Contributes to Disease-Inducing Mechanisms Resulting in Central Nervous System Autoimmune Disease, 173 J IMMUNOL 7070 (2004)("The central role of the innate immune system in the initiation and regulation of a subsequent Ag-specific immunity is becoming increasingly apparent . . . . It seems logical that this would also extend to the dysregulation of immunity to an autoantigen.")).

Ultimately, since he is not an immunologist, Dr. Renfroe finds the discussed articles "indicate that when authors are assessing for early response, immune responses can and do occur quickly." P Ex 33 at 2. Dr. Renfroe then defers to Dr. Byers regarding an explanation of "the factors which dictate why some patients fall into the extreme range of the standard bell shaped curve in the onset of their immune disorder" and regarding Ethan's specific rapid response. Id. With this report, it was still unclear what time frame Dr. Renfroe was opining was the start of Ethan's TM.

B. Expert Hearing Testimony

The Hearing was held on May 10 and 11, 2011. There were no objections to the four experts' qualifications to testify. Hr'g Tr. at 9, 80, 115, 179.

Dr. Renfroe testified first, specifically regarding Ethan's diagnosis and that his opinion was that Ethan "experienced a transverse myelitis shortly after a vaccine when he was four months old." Hr'g Tr. 10. Dr. Renfroe stated TM is a diagnosis made through clinical examination. Id.; see also P Ex 38 at 4, John H. Menkes, et al., CHILD NEUROLOGY (7th ed. 2006). Dr. Renfroe based his opinion that Ethan suffered TM upon the physical manifestation as recorded in the medical records as well as the impressions and treatment decisions his treating physicians made. Hr'g Tr. at 11.

Dr. Renfroe opined that the "first objective sign of [Ethan's] injury appeared" on December 19, six days after vaccination and when he was examined for the second time by his pediatrician, Dr. Frostad. Hr'g Tr. at 11-12; Hr'g Tr. at 24 (noting six days would be a medically appropriate time given a neurologist's understanding of TM literature). In his discussion of the time immediately following vaccination, Dr. Renfroe only vaguely referenced the symptoms averred by petitioner in her affidavit, the parents' hand-written symptom log found in the pediatrician's record, the parents' recitations of history to physicians, and the observations recalled by the pediatrician at the December 17 visit, as an initial illness after which evident paralysis was seen on December 19.

During cross-examination, Dr. Renfroe defended his opinion that the neurological injury presented objectively on December 19. Hr'g Tr. at 32-38. Upon questioning, Dr. Renfroe interprets the mother's description of Ethan in the days immediately following vaccination as symptoms of "an acute encephalopathy temporally associated with the administration of multiple

vaccines." Hr'g Tr. at 33-34. Dismissing the mother's observations of "limp noodle legs" as those of a mother very scared over her ill child and thus not reporting events accurately, Dr. Renfroe states he relies on the "first objective data," which is the pediatrician's note on December 19. Hr'g Tr. 34-36; Hr'g Tr. at 67 ("I can imagine this young lady who is scared to death. Her child is ill."). "I am very concerned about the emotional state of Momma having to provide these histories on a child who is now paraplegic." Hr'g Tr. at 41. The undersigned questioned Dr. Renfroe at the end of the first day of the Hearing about his reliance on some of the parents' observations while he dismissed other observations from them. Hr'g Tr. at 168. Dr. Renfroe explained that he was relying on the later observations as they seemed more contemporaneous to when the history was written. Id. He admitted that he ultimately did not know when the history was written. Id. He also admitted that he relied upon the pediatrician's records inconsistently as well. Id. at 168-69. In the end, Dr. Renfroe admitted he was concerned about the credibility of the information as it was relayed by the mother or the father. Id. at 169.

The description of Ethan getting better in the pediatrician notes, to Dr. Renfroe, is evidence of Ethan's acute encephalopathy resolving before the onset of neurological issues on December 19. Hr'g Tr. at 35. Respondent's counsel asked Dr. Renfroe, "[s]o, is it fair to say that you don't know when transverse myelitis started, you can only say when it was first documented on objective exam?" Hr'g Tr. at 35. To which, Dr. Renfroe agreed. Id. When confronted with the parents' history given when Ethan was hospitalized, Dr. Renfroe again did not find the symptoms of limp legs and inability to move the day after vaccination to be onset of TM. Hr'g Tr. at 36. Again, the undersigned noted that Dr. Renfroe was willing to accept the mother's report of limp legs the day after vaccination as a sign of an encephalopathy, but not as a sign of TM even when Dr. Renfroe noted that decreased movement of the legs is evidence of a spinal cord injury. Hr'g Tr. at 37. Dr. Renfroe seemed to attribute this to the lack of a more objective observation by a medical professional prior to December 19. Dr. Renfroe dismissed or would not accept the account, made non-contemporaneously, by the pediatrician on December 17. Hr'g Tr. at 38. When questioned further by respondent's counsel, Dr. Renfroe stated that the reports of limp legs or no movement in the legs prior to December 19 could possibly be the first symptoms of TM. Hr'g Tr. at 40-41.

Notably, Dr. Renfroe characterized the treating physicians' decision to withhold vaccinations from Ethan initially as being due to their concern regarding the vaccinations' possible causal connection to his TM. Hr'g Tr. at 19-20. When questioned about this characterization, Dr. Renfroe appeared to concede that Ethan's treating neurologist did not actually comment on vaccine causation; the treating doctor only noted the base temporal association. Hr'g Tr. at 20-21; but see infra p. 24-25 (discussing the fact that Ethan's treating neurologist held off on immunizations initially due to the potential immune compromise Ethan would have been under due to the IVIG treatments, not due to his concern about vaccine causation); Hr'g Tr. at 152.

Regarding whether vaccines in general can cause TM, Dr. Renfroe points to petitioner's Exhibit 40, the Agmon-Levin article. P Ex 40, N. Agmon-Levin, et al., Transverse myelitis and vaccines: a multi-analysis, 18 LUPUS 1198 (2009). Petitioner's Exhibit 40 is important to Dr. Renfroe because it shows an association between certain vaccines and reports of transverse myelitis, as well as the temporal association between vaccination and TM, which was between

several days and three months. Hr'g Tr. at 19 (citing P Ex 40 at 1). Discussing the potential mechanism, Dr. Renfroe specified the theory of molecular mimicry, wherein "[s]ome of the infectious agents or vaccines can have certain molecules that are similar to those in the central nervous system and so when challenged with an antigen they can develop antibodies against the central system. In this case probably myelin of some type." Hr'g Tr. at 21-22 (citing P Ex 20-C, RMS Riel-Romero, Acute transverse myelitis in a 7-month-old boy after diphtheria-tetanus-pertussis immunization, 44 SPINAL CORD 688 (2006); P Ex 38; P Ex 39, Douglas A. Kerr and Harold Ayetey, Immunopathogenesis of acute transverse myelitis, 15 CURRENT OPINION IN NEUROLOGY 339 (2002)).

The undersigned notes that the Kerr article discusses molecular mimicry, P Ex 39 at 4, but ultimately concludes, "it should be noted that extensive data continue to show overwhelmingly that vaccinations are safe and **are not associated with an increased incidence of neurological complications**." Further, "such case reports [of vaccine-induced autoimmunity] must be viewed with caution, as it is entirely possible that two events occurred in close proximity by chance alone." Id. at 3. In the discussion of molecular mimicry, Dr. Kerr only addresses the role of infections as a trigger for molecular mimicry. Id. at 4. When asked during cross-examination, Dr. Renfroe agreed that the implication of vaccine causation for Kerr was at least an open question. Hr'g Tr. at 45-46. The Menkes text, P Ex 38, also discusses molecular mimicry but only in relation to an antecedent illness or infection; it also only notes an "association" between TM and vaccinations for "rabies, tetanus toxoid, flu, measles, smallpox and hepatitis B." P Ex 38 at 3-4. Ethan did not receive these vaccines. The Riel-Romero article, P Ex 20-C, admits it is difficult to determine vaccine causation, discusses case reports of vaccine-associated TM and also suggests molecular mimicry as the immune-mediated process possibly triggered by the vaccine. P Ex 20-C at 3.

On re-direct, petitioner's counsel drew Dr. Renfroe's attention to the parents' history of Ethan's symptoms. P Ex 4 at 43. The distinction was shown between reports of "legs do not move at all, completely limp" on Thursday, December 15, and December 17 when the parents noted "wiggles leg when I tickle it (knee)." Id. Regarding this described change, Dr. Renfroe opined this was an improvement in the neurological picture, which would not be indicative of TM. Hr'g Tr. at 52-53. Dr. Renfroe described TM as a "mono-modal event." Hr'g Tr. at 53. If this description was accurate, Dr. Renfroe described the parents' observations as evidencing a "bi-modal" event, one with a peak of symptoms, then a drop, then another peak. Id. When questioned again by respondent, Dr. Renfroe again expressed doubt regarding the accuracy of the pediatrician's recollection of the December 17 exam when he dictated the note on January 10.[19] Hr'g Tr. at 59-60. And when asked by the undersigned about the parents' history included in the pediatrician records, Dr. Renfroe was unable to make sense of the symptoms as they relate petitioner's theory of an encephalopathy or other immune reaction right after vaccination followed by the onset of TM days later. Hr'g Tr. at 63-67. Ultimately, Dr. Renfroe admitted that he did not know how to interpret either the pediatrician's recollection of December 17 or the parents' history of events given to the pediatrician and that it was speculation to assume the mother was somehow hysterical and not reporting accurately. Hr'g Tr. at 67-70.

[19] As noted at other points in this Decision, other medical records and petitioner's own account of Ethan's symptoms provide a measure of corroboration for the content of this later-recorded exam note.

Dr. Byers testified next for petitioner. Dr. Byers testified that she was asked to review this case "to explain why the child had symptoms or lethargy and other symptoms that Dr. Renfroe characterized as an encephalopathy which occurred shortly after the vaccination. Probably, maybe 8 hours after the vaccination, maybe a little sooner and then resolved after about 72 hours." Hr'g Tr. at 81. Dr. Byers again relied upon Dr. Renfroe's opinion for the diagnosis of TM and for the association between Ethan's vaccines and his TM. Id. Dr. Byers described her impression of the course of events following Ethan's December 13 immunizations.

> Well, he basically had two sets of symptoms. The first set of symptoms are just the flu[] like symptoms that are characteristic of activation of the innate immune system after vaccination and those waned about maybe three days after his vaccination and then they seemed to merged into the transverse myelitis **which was documented to have begun around six days after vaccination.**

Hr'g Tr. at 81-82 (emphasis added). From this statement, it appears that Dr. Byers places onset of Ethan's TM by the physician's contemporaneous exam note alone, without addressing the parent's observations or the non-contemporaneously written December 17 exam note. She opined that the symptoms, characterized by Dr. Renfroe as an encephalopathy and by herself as activation of the innate immune system, began within the medically appropriate time frame following vaccination. Hr'g Tr. at 82. It was also her opinion that the beginning of the symptoms of TM days later is also an appropriate timeframe for that condition to be vaccine-related. This change is also indicative of a switch to the adaptive immune response. Id.

Dr. Byers then explained the innate and adaptive immune responses in relation to this case. The innate response is responsible for general inflammation that occurs in one's body, which acts to block invading viruses or bacteria. Hr'g Tr. at 83. The clinical expression for the innate immune response is what laypersons think of as "flu-like" symptoms: "anorexia,[20] malaise, fatigue, fever, myalgias, arthralgias, night sweats, weight loss and cachexia."[21] Hr'g Tr. at 84-85 (citing P Ex 40, Stephan R. Targan, INFLAMMATORY BOWEL DISEASE: FROM BENCH TO BEDSIDE (2nd ed. 2003)). Dr. Byers notes this can last up to 72 hours. Id. The innate response is also responsible for presenting the antigen, the offending organism, to the adaptive immune system, which creates the more tailored response to antigens. Id. Both the innate and adaptive immune responses involve proinflammatory cytokines. Id. at 84. Dr. Byers continued on, discussing the adaptive immune response as the more specific immune response that is responsible for dealing with organisms not already taken care of by the innate response. Hr'g Tr. at 86-87.

In Ethan's case, Dr. Byers testified that the following observations were consistent with the proinflammatory cytokine production of the innate immune response and could start within hours of receiving an antigen: temperature rise, eating poorly, difficulty swallowing, apathy,

[20] "Lack or loss of the appetitive for food." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 97 (31st ed. 2007).

[21] "A profound and marked state of constitutional disorder; general ill health and malnutrition." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 272 (31st ed. 2007).

poor suck reflex, and overall lethargy. Hr'g Tr. at 84-86. The undersigned notes that difficulty swallowing and poor suck reflexes do not appear in the cited Targan article, P Ex 42. Further, Dr. Byers does not address the parents' observations or the pediatrician's December 17 note of limp legs and lack of spontaneous movement in lower extremities in her interpretation of the initial symptoms Ethan suffered. When asked about involvement in the legs with an initial innate immune response, Dr. Byers stated:

> The way that I interpret it, it could [be] that basically this is just a very sick kid and all of those symptoms are – I think probably "a wet noodle" that probably mom found it off the internet but the child obviously was sick and had painful muscles probably all over not just the legs. It is just that you can most easily see the legs because if you tried to stand the child up or – the child was reluctant to stand up so it was easier to see in the legs.

Hr'g Tr. at 109.

Dr. Byers agreed with Dr. Renfroe in that the first objective neurological finding in Ethan presented on December 19, six days after vaccination. Hr'g Tr. at 87. In her opinion, six days is sufficient time for an adaptive immune response when the person had previously encountered the antigen. Dr. Byers referred to such secondary encounters as an anamnestic response, also referred to as "immunologic memory" or being primed. DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 74 (31st ed. 2007); see also, Hr'g Tr. at 89-90 ("An anamnestic response is a response that is occurring when the body has seen the antigen for a second, third, fourth time. In other words it is not the primary response."). She testified that with such a response, the person already had a population of T and B cells, which are components of the adaptive immune response. Hr'g Tr. at 88. In this case, Ethan received the vaccinations in questions on December 13 but also previously on October 12 of the same year. See, e.g., Hr'g Tr. at 90. Even assuming the pediatrician's December 17 recollected note was accurate in depicting neurological findings, Dr. Byers testified that this time period of four days after vaccination would still be an appropriate time for onset of TM, albeit "stretching the envelope." Id. at 87-88. The undersigned recalls another demyelinating-type case in which Dr. Byers testified before the undersigned that five days after vaccination was "a little bit too soon for a T-cell response to come up and actually start producing damage" even though the petitioner had received the same vaccine in the past and was presumably primed. Rego v. Sec'y of the Dept. of Health & Human Servs., No. 04-1734, 2008 WL 1990844 (Fed. Cl. Spec. Mstr. 2008). Dr. Byers also does not discuss whether the paraplegia started before the doctor actually observed Ethan, which is the logical course. A person has symptoms then visits a doctor; a patient does not begin having symptoms only when he or she first sees the doctor.

At this point in her testimony, Dr. Byers did not address the parent's report of "limp noodle" legs the day following vaccination. At Hearing, Dr. Byers and petitioner's counsel both referenced Dr. Rose's report wherein he noted an **adaptive response** needed at least four days in a person who has been previously primed to an antigen. Hr'g Tr. at 91 (citing R Ex E at 4)(emphasis added). Later in the testimony, Dr. Byers opined regarding an important distinction in this case; she stated one would expect an adaptive immune response to clinically manifest in a "primed" individual "[b]etween 1 and 2 weeks" following exposure to the antigen. Hr'g Tr. at

107. Again, the undersigned directs the reader to distinguish the experts' statements between initiation of an immune response and presentation of clinical symptoms that result from that immune response.

During cross-examination, Dr. Byers noted that the adaptive immune response was the response implicated in Ethan's TM. Hr'g Tr. at 93; supra p. 13 n. 17. She was asked whether she had the expertise to testify specifically regarding TM, to which Dr. Byers stated, "I would testify as to the etiology if I was asked to do so, but if I saw a child that had symptoms that would be, that could be, transverse myelitis I most certainly would refer them to a pediatric neurologist." Hr'g Tr. at 98. For purposes of this case, Dr. Byers accepted Dr. Renfroe's determination of the neurological symptoms. Hr'g Tr. at 98-99. However, Dr. Byers testified that the symptoms within a day of Ethan's vaccinations were an inflammatory response without differentiating between the flu-like symptoms and Ethan's lack of movement in his legs. Hr'g Tr. at 99. Regarding those first few days of symptoms, Dr. Byers agreed they were the evidence of common side effects of a properly working innate immune response but they were exaggerated in Ethan. Id. at 99-100. This assertion is countered by respondent's evidence that these non-specific symptoms can also be the presenting signs of the response that resulted in TM. Infra pp. 23. Referring to her expert report, respondent's counsel asked the expert how many days it would take for clinically observable symptoms of an adaptive immune response to show. Hr'g Tr. at 100-01. Rephrasing the question, which may be noteworthy in this case, Dr. Byers stated that "[i]t takes four to seven days for the vaccination to result in activation of the adaptive immune system resulting in an autoimmune disease." Hr'g Tr. at 101. The following exchange then occurred:

> Respondent's counsel: So, if the Special Master were to find that Ethan's transverse myelitis **began before four days** then you would not be able to opine that his transverse myelitis was as a result of vaccination.
> Dr. Byers: I don't know if I would not be able to opine but I can certainly tell you that as I sit here today I would not be able to opine.
> The court: And that is because that would no longer be an appropriate time frame?
> Dr. Byers: It is because it would – you would have to invoke additional complicating factors which is not present in this child for that timeframe to be operative.

Hr'g Tr. at 101-02 (emphasis added). Further, Dr. Byers agreed that onset of TM would be too early if the court assumed the history given in Dr. MacDonald's notes is accurate, those being the acute weakness in the legs actually began on the day of Ethan's vaccinations. Hr'g Tr. at 108; see, e.g., P Ex 10 at 35. Ultimately though, Dr. Byers stated:

> It is my opinion that all of the symptoms that occurred within the first 72 hours of vaccination were due to the innate immune system and that the subsequent clear emergence of the TM was due to the adaptive immune system.

Hr'g Tr. at 110.

Dr. Sladky, respondent's pediatric neurologist, testified next. Hr'g Tr. at 112-62.[22] Dr. Sladky summarized his opinion in this case by stating, "the timeframe from the vaccination to the onset of clinical symptoms is incredibly short to be a plausible side-effect from the vaccine." Hr'g Tr. at 115-16. Dr. Sladky discussed TM generally and stated that he does not find one can diagnose Ethan absolutely with TM. Hr'g Tr. at 116-18. Even though Dr. Sladky still considered a spinal infarct possible, as opposed to the diagnosis of a demyelinating injury or TM, he noted that infarct is an even rarer condition than TM in children. Hr'g Tr. at 118. "So, I think we can exclude a spinal cord tumor, a spinal cord hemorrhage but I don't think one can clearly distinguish transverse myelitis from a spinal cord infarct as the cause of this child's generic myelopathy." Id. In a discussion related to Ethan's normal diagnostics, Dr. Sladky admitted that some cases of TM would present with normal findings on neuroimaging and cerebral spinal fluid analysis ("CSF"). Hr'g Tr. at 118-120 (noting that it would be more likely to have normal test results in the scenario of a spinal infarct). Regarding Ethan's clinical presentation, he opined the ultimate cause of Ethan's myelopathy could be either spinal infarct or TM based on those observations. Hr'g Tr. at 120. Respondent's counsel asked Dr. Sladky if he took issue with the diagnosis of TM, and Dr. Sladky found the evidence between TM and spinal infarct to be "a wash." Hr'g Tr. at 122. "[I]f you were to bet the odds, transverse myelitis is a more common cause of myelopathy in a four month old probably than spinal cord stroke . . . ." Id. Dr. Sladky did add, however, that based upon odds, it would be atypical for a child to have normal diagnostics with TM. Hr'g Tr. at 122-23.[23]

In contrast to Dr. Renfroe's characterization and dismissal of the parent's report of symptoms following vaccination, Dr. Sladky found the parent's description to be "a really eloquent lay-person description of acute spinal cord injury." Hr'g Tr. at 125.

Dr. Sladky explained what occurs with an acute spinal cord injury: "what is unique about the acute phase is you develop what is called spinal shock." Hr'g Tr. at 125. In spinal shock, a patient suffers "flaccidity in the extremities so things go completely limp . . . ." Id. "As the spinal shock wears off, which happens over hours to days, you begin to see a more typical long term pattern with increased muscle tone as opposed to limp noodle, [with] increased reflexes and increased reflex responsiveness to stimulation." Hr'g Tr. at 125-26. Examining the parents' notes, "she describes on day one after vaccination [] limp noodle legs, on day two the legs don't move at all. . . . By about day three or four the legs start to show some spontaneous movement, the spinal shock is wearing off." Hr'g Tr. at 126. When the parent describes the child's legs pulling away when the foot is touched, Dr. Sladky noted a neurologist would question if this was spinal shock wearing off and reflexive or whether this was actual volitional movement. Id. He stated he could not say definitively at the time if this was spinal shock wearing off or volitional movement; however, it was "**a classic description of acute spinal cord injury with transient spinal shock followed by recovery with increased muscle tone and increased reflexes.**" Hr'g

[22] The Hearing Transcript mistakenly references Dr. Sladky as "Dr. Slanky."

[23] At this point in his testimony, Dr. Sladky also discussed the complication of the mother's Factor V Leiden mutation and its potential effect on Ethan as it relates to the diagnosis of a spinal infarct. Hr'g Tr. at 123-24. Given the undersigned's review of the entire record, a thorough exposition of this issue is unnecessary in light of the ultimate finding for petitioner that the evidence preponderates in favor of petitioner's allegation – that Ethan suffered TM.

Tr. at 126-27 (emphasis added). "Then looking in retrospect in the long term that is exactly what this child is left with." Hr'g Tr. at 127.

With Dr. Sladky, the undersigned discussed his reliance upon parental histories in his own practice. Hr'g Tr. at 158. Dr. Sladky responded that although parents may be distraught or distracted, they can often provide valuable and subtle information about what is happening to a child. Hr'g Tr. at 158-59. Dr. Sladky actually stated he would rely more upon the parents' recitation of events than on the pediatrician's recollected note of the December 17 examination. Hr'g Tr. at 160. When questioned by petitioner's counsel, Dr. Sladky was unable to quantify a percentage or whether it was typical for a child with TM to present with spinal cord shock. Hr'g Tr. at 139-40. A piece of medical literature submitted in this case explains that spinal shock is severe in two thirds of TM patients. R Ex B-10 at 2, Maria José Sá, Acute transverse myelitis: A practical reappraisal, 9 AUTOIMMUNITY REVIEWS 128 (2009).

Dr. Sladky held the opinion that this description of events was not two separate illnesses or immune responses. Hr'g Tr. at 127. Also, "80% of children with transverse myelitis will have pain. And so in a child who is developing transverse myelitis[,] crankiness, irritability, fussiness, could certainly be manifestations of pain typical of the illness itself." Id. at 128. Regarding whether or not the first symptoms following vaccination were an encephalopathy, Dr. Sladky was very doubtful. "I really don't know how to apply the term encephalopathy to the symptoms that are described by the Mom. You know fussy, irritable, cranky is fine but I don't hear any evidence of a defused disorder of consciousness, an inability to respond to his environment." Hr'g Tr. at 128. In contrast to the theory of encephalopathy, "the evolution of the symptoms was entirely consistent with an acute myelopathy whether it be due to infarct or transverse myelitis." Id. When the signs of encephalopathy were discussed during cross-examination, Dr. Sladky noted that the signs, other than the lower extremity paraplegia, were non-specific signs of illness or feeling poorly that one could attribute to a normal vaccine response or development of TM. Hr'g Tr. at 138-39.

Later in his testimony, Dr. Sladky returned to the presentation of symptoms observed by Ethan's parents. Respondent's counsel asked, "in your clinical experience with TM, is a layman's wording of limp noodle legs, is that consistent with clinical transverse myelitis?" Hr'g Tr. at 136. Dr. Sladky replied, "[t]hat is classic . . . ." Id. When asked if "limp noodle legs" was a presentation of neurologic process, he stated, "[w]hen you are seeing the marked disparity between function in the arms and the legs you have an internal comparator and absolutely if the legs aren't moving and the arms are moving[,] something bad is happening in between and that means the spinal cord." Hr'g Tr. at 136-37.

Regarding the timing of onset of symptoms, Dr. Sladky discussed the difficulty in determining the appropriate time between a potentially causative event and the onset of TM. Hr'g Tr. at 129-30. Relying on an animal model, Dr. Sladky agreed with Dr. Byers' testimony that one to two weeks is the shortest time seen between immune stimulus and the onset of disease; with this statement, Dr. Sladky did not differentiate whether this was the time frame for a primed or unprimed individual. Hr'g Tr. at 130-31. "You can do some manipulations of the experimental paradigms in order to try and decrease it **but you really can't get it below four to five days at the absolute minimum and even that is extraordinarily difficult**." Hr'g Tr. at

131 (emphasis added). Dr. Sladky suggested that the observation of clinical symptoms means the person was exposed to the antigen, it was identified by the body, reacted to the antigen for cross reacting and the antibodies migrated into the spinal cord and caused the damage seen clinically. Hr'g Tr. at 130. "I don't think that [] can happen in under a minimum of five days and then maybe not even that short . . . But [nonetheless,] this timeframe is absolutely inconceivable." Id.

Dr. Renfroe, petitioner's expert neurologist, had relied upon an article presenting the animal model discussed by Dr. Sladky at the Hearing. P Ex 33-B, F.L. Gordon, et al., Rapid Entry and Downregulation of T Cells in the Central Nervous System During the Reintroduction of Experimental Autoimmune Encephalitis, 12 (1-2) J OF NEUROIMMUNOLOGY 15 (2001). Dr. Sladky praised the article, explained the genesis of the Experimental Autoimmune Encephalomyelitis ("EAE") model and gave context to how this affects the way a doctor or scientist must view the timing of onsets discussed in the paper. Hr'g Tr. at 132-35. Particularly, the cells of the adaptive immune system themselves are introduced into the animal being observed and those cells had already progressed through thirteen days development since their initial exposure to the antigen in another animal. Hr'g Tr. at 135. "So, this is like offering someone an opportunity to start a 100 mile race at mile 75." Id. Dr. Sladky accepted the fact that this article showed it took thirteen plus four days to cause observable injury. Hr'g Tr. at 136. "This rat did not suddenly get exposed to an antigen and within four days [was] dragging its legs around." Id. at 136.[24]

On cross-examination, Dr. Sladky was asked if the animal model discussed would be representative of what occurs when a human's immune system is already primed or previously exposed to an antigen. Hr'g Tr. at 148-50. Dr. Sladky answered that this was not the case; in the animal model discussed in petitioner's Exhibit 33-B, the responding cells were not created by the host's system, nor were they merely memory cells from previous exposure. Hr'g Tr. at 149-150. The cells injected into the animal were not waiting around for instigation; they were active "killer cells" that were a step beyond simply being primed and were actively responding. Id. Dr. Sladky was also asked by petitioner's counsel if he accepted Dr. Rose's estimate on the timing of onset, which was that it required a minimum of four days to instigate an adaptive immune response. Hr'g Tr. at 150-51. Dr. Sladky appeared to reluctantly accept Dr. Rose's opinion on timing but qualified it by noting his belief that Dr. Rose's opinion on the minimum time requirement was generous, giving considerable latitude to the lower limit of acceptability. Hr'g Tr. at 151.

Petitioner's counsel also drew Dr. Sladky's attention to a report by the Institute of Medicine ("IOM"), which stated "a conservative estimate of the limits of the latencies for both GBS and ADEM[, both demyelinating conditions,] is considered to be from five days to six weeks." Hr'g Tr. at 150 (citing R Ex A-5 at 45). Dr. Sladky accepted this evidence on timing. Hr'g Tr. 150-51. On re-direct, respondent's expert asked Dr. Sladky his interpretation of the use of the word "conservative" in the IOM's statement, Hr'g Tr. at 157, to which Dr. Sladky

[24] Dr. Rose confirmed and reiterated the process by which researchers in the Gordon article, P Ex 33-B, came about producing the animal model of the demyelinating autoimmune disorder, which involved first exposing one animal to myelin for thirteen days, extracting the developed T cells and further activating them, then injecting those active T cells into a naïve animal and observing the onset of clinical symptoms three to four days. Hr'g Tr. at 189-93.

responded that the estimates were beyond what one would normally consider, that the lower limit was lower and the higher limit higher than what they likely are – "generously broad." Id.

Petitioner's counsel discussed potential mechanisms with Dr. Sladky and Dr. Sladky agreed that molecular mimicry was a means by which autoimmunity to TM could occur. Hr'g Tr. at 148. Counsel also asked about the treating neurologist's note to withhold vaccines from Ethan; Dr. Sladky responded, "[w]hat Dr. McDonald said in his note was that because of the IVIG and the Methylpredisolone that his immu[ne] response to a vaccine would not be – would be compromised and that it would be reasonable to wait six months to go ahead and give it to him." Hr'g Tr. at 152.

On the second day of the Hearing, Dr. Rose testified as respondent's immunologist. Hr'g Tr. at 176-231. Dr. Rose began by noting his reliance on Dr. Sladky for the characterization of Ethan's symptoms following the vaccination, including the timing of when Ethan's myelopathy began. Hr'g Tr. at 180. Later on he stated that he held no opinion regarding whether Ethan suffered from TM or from a spinal cord infarct but was testifying upon the assumption that Ethan suffered TM. Hr'g Tr. at 184-85.

Dr. Rose briefly detailed the innate and adaptive immune responses, which was ostensibly in agreement with the description given by Dr. Byers. Hr'g Tr. at 180-81. He explained that TM is generally regarded as an autoimmune condition and a product of the adaptive immune system. Id. at 181-82. In light of how the adaptive immune response works, it is unreasonable to conclude that TM could occur within 24 hours of vaccination, if it was vaccine-caused. Id. at 182. "[T]his is the result of an adaptive immune response and it takes a number of days for such a response to be mounted." Id. at 182. Dr. Rose provided a detailed explanation of the processes of the adaptive immune response that need to take place before one would see clinically observable signs of an autoimmune condition. Hr'g Tr. at 182-84. See also Contreras v. Sec'y of the Dept. of Health & Human Servs., No. 05-626V, 2012 WL 1441315, *9-12 (Fed. Cl. Spec. Mstr. Apr. 5, 2012)(discussing in-depth the multiple steps needed for a neurological injury caused by molecular mimicry, offered by experts for both petitioner and respondent), appeal docketed, No. 05-626V (Fed. Cl. May 4, 2012).

Regarding the timing of the mechanisms discussed, Dr. Rose elucidated an extremely important point in this case. Supra p. 8. He explained that there is a difference between development of an autoimmune response – the creation and presence of auto-antibodies[25] by the adaptive immune system – and manifesting the detectable signs of an injury caused by the autoimmune response – what signs and symptoms a doctor or patient can observe or what a patient notices that brings him to the doctor in the first place. Hr'g Tr. at 186-89.[26] The clinical manifestation of the autoimmune response, the "visible" signs and symptoms, "**can be a few days, 4, 5, or 6 days after the autoimmune response is evident.**" Hr'g Tr. at 186 (emphasis added). If the host was not primed for the antigen, Dr. Rose testified that the autoimmune

[25] Auto-antibodies are "antibodies directed to the molecule in the host . . . ." Hr'g Tr. at 186.

[26] In her Post-Hearing Brief, petitioner references the time interval necessary for an adaptive immune response without differentiating between that and the manifestation of clinical symptoms following that adaptive immune response. P Post-Hearing Brief at 33-34.

response would manifest in 9 to 20 days. Hr'g Tr. at 184. However, Dr. Rose was careful to note that this 9 to 20 day time frame was not the time frame in which the clinical symptoms actually arose. Hr'g Tr. at 185-86. He noted it would take days beyond the manifestation of the autoimmune response before the injury, here TM, became evident. Id. In a host that was previously exposed to the antigen or primed, Dr. Rose noted the time frame in which the clinical signs manifest can be "significantly shortened." Hr'g Tr. at 185.

With that context, respondent's counsel asked Dr. Rose about the statement in his report, R Ex B, that initiation of the adaptive immune response can be hastened but still requires at least 96 hours. Hr'g Tr. at 187-88 (quoting P Ex B at 4). He even characterized 96 hours as the "most generous" time frame in which one could detect an adaptive response in a primed host. Hr'g Tr. at 188. As stressed previously, this time frame is different from and shorter than the time in which symptoms would clinically manifest and the patient or physician would know a disease is underway. Id. at 188-89.

At this point, respondent's counsel took Dr. Rose through the article, P Ex 33-B, which discussed EAE, the animal-model demyelinating disease. Hr'g Tr. at 189-94. Specifically regarding the author's reference to a three to four day onset of clinical symptoms, Dr. Rose reiterated the explanation of the animal model given by Dr. Sladky, which was that the rats that had suffered effects in three to four days were injected with already-developed, already-activated T cells. Hr'g Tr. at 190. Dr. Rose referred to these T cells as "fully developed . . . [and] further activated . . . [and] they were very, very active T cells and then they transferred them to a naïve recipient." Hr'g Tr. at 190-92. Later during cross-examination, Dr. Rose noted the recipient was not merely injected with cells with a memory of the antigen – myelin – but the animal was injected with super activated cells with that memory, thus hastening clinical manifestations of the disease. Hr'g Tr. at 204-07. The clinical symptoms arising three to four days after injection were due to injection of large numbers of fully developed, fully activated T cells already seeking out myelin, not simply injecting another antigen that acts as a molecular mimic to myelin. Hr'g Tr. at 192. Dr. Rose described the three to four day reference as the time between "the already developed [auto]immune response which was present in the donor rat and the actual appearance of clinical disease in the naïve recipient rat." Id. The three to four days, in other words, was the time it took the already-developed autoimmune response to damage the myelin coating of the nerves and cause observable symptoms. Hr'g Tr. at 206. As explained later in his testimony, it would take approximately 96 hours to develop a measurable autoimmune response in a person already primed, and then an additional amount of time thereafter, perhaps four days with a condition such as TM, to see the effects or clinical symptoms of that autoimmune response – the actual damage of the disease. Hr'g Tr. at 208-15; Hr'g Tr. at 227-29 (noting the donor rat was exposed to the antigen for ten days to initiate an immune response, after which the T cells are harvested, activated further and put into the recipient rat, which suffered the clinical symptoms of the disease in three to four days after injection). In terms of this case, assuming petitioner's experts' opinions of the onset occurring approximately four days after vaccination, Dr. Rose testified that even four days is simply too short of a time period for the vaccine to be the cause of Ethan's TM. Hr'g Tr. at 226-27. Relying upon the animal model and the time taken to develop the T cells in the first animal, a six day onset of Ethan's TM, this timing would also be too short. Hr'g Tr. at 226-27; see infra pp. 46.

During cross-examination, Dr. Rose was directed to examine the Frohman article submitted by respondent. Hr'g Tr. at 216-19 (discussing P Ex B-8, Elliott M. Frohman and Dean M. Wingerchuk, Transverse Myelitis, 363 NEJM 564 (2010)). Petitioner's counsel questioned Dr. Rose regarding the author's statement that TM is an autoimmune phenomenon that can occur after vaccination. Hr'g Tr. at 217. Dr. Rose stated, "I agree it can. I don't know of any evidence that it does." Hr'g Tr. at 218. Dr. Rose continued by emphasizing that co-occurrence of events does not necessitate one caused the other. Hr'g Tr. at 218-19.

Finally, questioning of Dr. Rose concluded with some questions from the undersigned and clarification from the parties' counsel. Hr'g Tr. at 224-31. When asked if "limp noodle legs" would be a manifestation of an innate immune response to the vaccinations, Dr. Rose stated, "I can't answer that. I don't know what would have caused these noodle-like legs" and that it did not make sense to him to implicate the innate immune system as responsible for Ethan's leg involvement. Hr'g Tr. at 224-26.

V. LEGAL STANDARD

In Vaccine Act cases, causation can be established either through the statutorily prescribed presumption of causation or by proving causation in-fact. For presumptive causation claims, the Vaccine Injury Table lists certain injuries and conditions, which create a rebuttable presumption that the vaccine caused the injury or condition if they are found to occur within a prescribed time period. §14(a); 42 C.F.R. § 100.3. Petitioner here argues the vaccinations in-fact caused her son's injury, a so-called "off-Table" case. See P Post Hearing Memorandum at 3, filed Apr. 8, 2011 ("In the instant case, petitioners [sic] have proceeded under a non-"table" theory").

According to §13(a)(1)(A), claimants must prove their case by a preponderance of the evidence.[27] To demonstrate entitlement to compensation in a causation in-fact case, petitioner must affirmatively demonstrate by a preponderance of the evidence that the vaccination in question more likely than not caused or significantly aggravated the injury alleged. See, e.g., Grant v. Sec'y of Dept. of Health & Human Servs., 956 F.2d 1144, 1146, 1148 (Fed. Cir. 1992); Bunting v. Sec'y of Dept. of Health & Human Servs., 931 F.2d 867, 872 (Fed. Cir. 1991); Hines v. Sec'y of Dept. of Health & Human Servs., 940 F.2d 1518, 1525 (Fed. Cir. 1991); see also §§11(c)(1)(C)(ii)(I) and (II). To prevail, petitioner must produce "preponderant evidence both that [the] vaccinations were a substantial factor in causing the illness, disability, injury or condition and that the harm would not have occurred in the absence of the vaccination." Pafford v. Sec'y of Health and Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006) (citing Shyface v. Sec'y of Health and Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999)). The vaccination "must be a 'substantial factor'" in bringing about the injury, but "it need not be the sole factor or even the predominant factor." Id. at 1357 (quoting Shyface, 165 F.3d at 1352-53).

[27] A preponderance of the evidence standard requires a trier of fact to "believe that the existence of a fact is more probable than its nonexistence before the [special master] may find in favor of the party who has the burden to persuade the [special master] of the fact's existence." In re Winship, 397 U.S. 358, 371-72 (1970)(Harlan, J. concurring)(quoting F. James, CIVIL PROCEDURE, 250-51 (1965)). Mere conjecture or speculation will not establish a probability. Snowbank Enter. v. United States, 6 Cl. Ct. 476, 486 (1984).

In Althen v. Sec'y of Dept. of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005), the Court of Appeals for the Federal Circuit explained that petitioner's burden is to produce "preponderant evidence" demonstrating: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccination and injury."

The evidence relating to these three prongs "must cumulatively show that the vaccination was a 'but-for' cause of the harm, rather than just an insubstantial contributor in, or one among several possible causes of, the harm." Pafford, 451 F.3d at 1355. Petitioner must provide a "reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly v. Sec'y of Dept. of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2005); Broekelschen v. Sec'y of the Dept. of Health & Human Servs., 618 F.3d 1339, 1350 (Fed. Cir. 2010), reh'g en banc denied (Dec. 8, 2010). Petitioners do not satisfy this burden by merely showing a proximate temporal association between the vaccination and the injury. Grant, 956 F.2d at 1148 (quoting Hasler v. United States, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984) (stating "inoculation is not the cause of every event that occurs within the ten day period [following it]. . . . Without more, this proximate temporal relationship will not support a finding of causation")); Hodges v. Sec'y of the Dept. of Health & Human Servs., 9 F.3d 958, 960 (Fed. Cir. 1993). Also, petitioners do not demonstrate actual causation by solely eliminating other potential causes of the injury. Grant, 956 F.2d at 1149-50; Hodges, 9 F.3d at 960.

Petitioners must support their proposed causation theory with a "sound and reliable medical or scientific explanation." Knudsen v. Sec'y of the Dept. of Health & Human Servs., 35 F. 3d 543, 548 (Fed. Cir. 1994).[28] As the Federal Circuit reiterated:

[28] The general acceptance of a theory within the scientific community can have a bearing on the question of assessing reliability while a theory that has attracted only minimal support may be viewed with skepticism. Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 594 (1993). Although the Federal Rules of Evidence do not apply in Program proceedings, the United States Court of Federal Claims has held that "Daubert is useful in providing a framework for evaluating the reliability of scientific evidence." Terran v. Sec'y of Dept. of Health & Human Servs., 41 Fed. Cl. 330, 336 (1998), aff'd, 195 F.3d 1302, 1316 (Fed. Cir. 1999), cert. denied, Terran v. Shalala, 531 U.S. 812 (2000). See also Cedillo v. Sec'y of Dept. of Health & Human Servs., 617 F.3d 1328, 1338-39 (Fed. Cir. 2010)(approving the use of the Daubert factors in examining the reliability of expert testimony); Moberly v. Sec'y of Dept. of Health & Human Servs., 592 F.3d 1315, 1324 (Fed. Cir. 2010)(citing Daubert; approving of the use of the Daubert factors in determining expert reliability). In Daubert, the Supreme Court noted that scientific knowledge "connotes more than subjective belief or unsupported speculation." Daubert, 509 U.S. at 590. Rather, some application of the scientific method must have been employed to validate the expert's opinion. Id. In other words, the "testimony must be supported by appropriate validation – i.e., 'good grounds,' based on what is known." Id. Factors relevant to that determination may include, but are not limited to:

> Whether the theory or technique employed by the expert is generally accepted in the scientific community; whether it's been subjected to peer review and publication; whether it can be and has been tested; and whether the known potential rate of error is acceptable.

Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1316 (9th Cir. 1995)(Kozinski, J.), on remand from, 509 U.S. 579 (1993); see also Daubert, 509 U.S. at 592-94.

> Although Althen and Capizzano make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury. See Daubert, 509 U.S. at 593-97, 113 S.Ct. 2786 (noting that one factor in assessing the reliability of expert testimony is whether the theory espoused enjoys general acceptance within a relevant scientific community). . . . Althen makes clear that a claimant's theory of causation must be supported by a "reputable medical or scientific explanation." 418 F.3d at 1278.

Andreu v. Sec'y of Dept. of Health & Human Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); see also Grant, 956 F.2d at 1148 ("A reputable or scientific explanation must support this logical sequence of cause and effect."). The Federal Circuit further explained in Andreu:

> The assessment of whether a proffered theory of causation is "reputable" can involve assessment of the relevant scientific data. Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard . . .

Andreu, 569 F.3d at 1380 (citing Bunting, 931 F.2d 867, 873 (Fed. Cir. 1991)). Proving causation in-fact by proving the Althen standards requires preponderant proof of each of the three prongs. de Bazan v. Sec'y of the Dept. of Health & Human Servs., 539 F.3d 1347, 1351-52 (Fed. Cir. 2008); Moberly, 592 F.3d at 1315, 1322; Caves v. Sec'y of the Dept. of Health & Human Servs., 100 Fed. Cl. 119, 132 (Fed. Cl. 2011) aff'd per curiam, No. 2011-5108, 463 F. App'x 932, 2012 WL 858402 (Fed. Cir. Feb. 14, 2012).

A finding that petitioners established their *prima facie* burden does not end the inquiry. The Act provides that a petitioner may not receive compensation "if the court finds by a

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However, the court also cautioned about rejecting novel scientific theories that have not yet been subjected to peer review and/or publication. The court pointed out that the publication "does *not* necessarily correlate with reliability," because "in some instances well-grounded but innovative theories will not have been published." Daubert, 509 U.S. at 593. However, the Supreme Court has provided guidance to the lower courts in determining the reliability of a novel proposition:

> [S]ubmission to the scrutiny of the scientific community is a component of "good science," in part because it increases the likelihood that substantive flaws in methodology will be detected. (citation omitted). The fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology on which an opinion is premised.

Id. at 593-94; see Althen v. Sec'y of Dept. of Health & Human Servs., 418 F.3d 1274,1280 (Fed. Cir. 2005)("the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."); see also, Gall v. Sec'y of Dept. of Health & Human Servs., No. 91-1642V, 1999 WL 1179611, at *8 (Fed. Cl. Spec. Mstr. Oct. 31, 1999).

preponderance of the evidence on the record as a whole 'that the illness, disability, injury, condition, or death described in the petition is due to **factors unrelated to the administration of the vaccine** described in the petition.'" Knudsen, 35 F.3d at 547 (citing §13(a)(1)(B))(emphasis in original); Walther v. Sec'y of the Dept. of Health and Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007)("[W]e conclude that the Vaccine Act does not require petitioner to bear the burden of eliminating alternative causes when the other evidence on causation is sufficient to establish a prima facie case."). Since the undersigned finds that petitioner hase not provided preponderant evidence on vaccine causation, a factor unrelated analysis is unnecessary.

VI. DISCUSSION

Two factual issues are presented herein, with one proving to be highly critical in resolving this case. First, there was dispute between the parties regarding the proper diagnosis of the injury suffered by Ethan. However, the second factual issue of the date of onset of Ethan's alleged injury proves to be a deciding factor of petitioner's claim. Where the preponderance of evidence lies with regard to the first question, Ethan's diagnosis, is relatively easy to determine. Based on the treating doctors' assessments and treatment choices found in the medical records, bolstered by evidence discussed by both parties' experts, the undersigned finds Ethan suffered an inflammatory, demyelinating process of his spinal cord, most likely transverse myelitis. The injury is discussed and will be referred to as transverse myelitis or TM throughout. The second question regarding the onset of Ethan's TM, based upon the medical records and petitioner's affidavit appears somewhat straightforward, but Dr. Renfroe argues strenuously to the contrary. The undersigned finds that the neurological symptoms of Ethan's injury began within approximately 24 hours after vaccination based on petitioner's affidavit, the parents' reports, the treating physicians' recorded histories and the testimony of respondent's experts. Petitioner's experts were unable to persuasively contend with this information and were unable to produce preponderant evidence that Ethan's TM began at a later point.

The issue of timing is decisive as petitioner's experts could not support vaccine causation if onset of Ethan's TM was within 24 hours of his vaccinations. With this finding of onset within 24 hours, petitioner fails to meet Althen prong III. Due to the decisive factual finding regarding onset, much of the causation discussion in this case took on a secondary role. However, the undersigned briefly discusses the state of evidence had petitioner been able to show a later onset. Even assuming a later onset, it is not clear that petitioner's evidence reaches a preponderant level regarding causation. This Decision begins with the factual findings and then reviews the evidence as viewed through the prongs set forth in Althen.

A. DIAGNOSIS OR IDENTIFICATION OF THE INJURY

Despite contentions raised by respondent, the undersigned does not find difficulty in determining the diagnosis of the injury for purposes of this litigation. Despite the lack of diagnostic findings, Ethan's treating physicians proceeded under the presumption that he suffered from a demyelinating injury localized in his spine and often referred to this condition as transverse myelitis throughout the medical records. Other injuries were considered in Ethan's differential diagnosis, but ultimately he was treated for a demyelinating spinal injury. References to this type of injury, and to TM specifically, were continued through his medical

history by his pediatrician, neurologist and other medical providers.[29] Additionally, petitioner's experts agreed with the diagnosis of TM. Although respondent's expert neurologist questioned the possibility of a spinal stroke or infarct, he did not disagree with the diagnosis. When asked whether he felt it was TM or a spinal stroke, Dr. Sladky stated, "[i]t could go either way." Hr'g Tr. at 120. Furthermore, as attested by both expert neurologists in this case, Ethan's clinical presentation is consistent with TM. The undersigned finds the impressions of the treating physicians to be highly relevant and persuasive with regard to this issue. Capizzano v. Sec'y of the Dept. of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006). Based on the totality of the evidence, the undersigned finds Ethan suffered a demyelinating spinal injury subsequent to his December 13 vaccinations, referenced herein as TM.[30]

B. ONSET AND TIMING OF THE INJURY

The matter of when Ethan's TM symptoms arose is slightly more difficult than the issue of the proper injury. Petitioner contends onset of Ethan's TM occurred around six days after vaccination, reasoning the symptoms prior to this were due to an encephalopathy or an exaggerated innate immune response. Respondent asserts Ethan's TM began within 24 hours, when he awoke the day following vaccination with the "limp noodle" legs, and the entire subsequent course of events was consistent with development of TM. As discussed, the undersigned finds onset of Ethan's TM began within 24 hours, when he awoke on December 14, 2005. The undersigned will briefly review the evidence the parties draw upon for their arguments regarding timing and then discuss the weight of the parties' arguments.

1. Five general areas of evidence the parties draw upon for onset

There are five general sources from which evidence regarding onset is presented in this case. Most of those sources are not in conflict. As this evidence was set forth above, it will not be recited in full detail. Considering the record in its entirety, preponderant evidence demonstrates the onset of Ethan's TM occurred within approximately 24 hours, observed by his parents when Ethan awoke on December 14, 2005.

First, petitioner presents evidence in the form of the factual observations from Ethan's parents, as evidenced in petitioner's affidavit, P Ex 16, and the parents' written symptom history, which is included in the pediatric records. P Ex 4 at 43; see supra pp. 3-4.

Petitioner's affidavit is unequivocal: "The next morning his legs were like limp noodles, and he was unable to move them." P Ex 16. Petitioner goes on to discuss the other symptoms

[29] Review of medical records shows this is **not** a case where the vaccinee or his parents, as lay persons, asserted an injury and that assertion was carried through the medical records by unquestioning medical professionals. See Veryzer, No. 06-522V, 2011 WL 1935813, *17, aff'd, 100 Fed. Cl. 344, 355, appeal docketed, No. 12-5034 (Fed. Cir. Jan. 3, 2012).

[30] The undersigned acknowledges respondent's evidence regarding spinal stroke or infarct and the role of the Factor V Leiden mutation; however, as preponderant evidence shows Ethan suffered from TM or a very similar injury, the undersigned finds it unnecessary to present a full discussion and analysis of this rebuttal or factor unrelated evidence.

Ethan suffered and noted, "[t]hese symptoms continued for several days. He slowly improved **but still couldn't move his legs** . . . ." Id. (emphasis added).

In the recollected note from Ethan's pediatrician regarding the December 17 exam, the pediatrician noted Ethan's father was to "write down a log of this baby's behaviors every day since the illness started." P Ex 4 at 45. As discussed above, this parental history of events was included in the pediatrician's records. P Ex 4 at 43-44 ("this is documented well by parents' history they bring in"). On Wednesday, December 14, 2005, the parents describe the "limp noodle legs" among Ethan's other, nonspecific symptoms. Id. at 43. On days three, four, five and six after vaccination, it appears the parents observed some change in Ethan's leg activity, most notably Ethan's reflex responses to pinching or tickling. The interpretation of the parents' history was discussed at length by the experts.

As presented previously, petitioner argues the early symptoms were due to a normal but perhaps exaggerated innate immune response to the vaccinations or an encephalopathy, which was resolving and unrelated to the process resulting in TM. Like an encephalopathy, an exaggerated immune response is not discussed in the medical records or seen by the opposing experts. Supra pp. 3-4, 14-15, 23; R Ex B at 4. It is not noted in his medical records that Ethan ever presented with other unusual or exaggerated immune responses to previous infection or vaccination. No medical literature or other reliable support was submitted that would support the exaggerated immune response proposition either. This argument, that Ethan suffered an exaggerated immune response, was poorly developed. Infra p. 39 (discussing the allegation of an exaggerated immune response in greater detail).

Respondent's expert neurologist specifically does not agree with petitioner's experts' interpretation of events and does not observe the significant changes in Ethan's condition as petitioner characterizes them. He opines the changes were likely spinal shock, which is an acute, initial onset of a TM injury that evolves into the more stable presentation of the TM symptoms. Hr'g Tr. at 125-26. Respondent's Exhibit B-10 supports this description of TM onset. Infra pp. 35. Dr. Sladky testified that the parents' description of events found in petitioner's affidavit and the hand-written notes in the pediatric records were entirely consistent with the TM disease process. E.g., Hr'g Tr. at 125, 158-60.

Second, petitioner offers medical histories and physicians' observations found in the medical records, most notably from Ethan's pediatrician, P Ex 4, and his treating neurologist, P Ex 8.[31] Exhibit 4 contains Ethan's pediatric records. At the time of the vaccinations, the

[31] There are other, later references in the medical records to the timing of onset of Ethan's paraplegia. See also, P Ex 12 at 1 ("Mom has some concerns with [TM] being associated with his immunizations due to the timing. He had **received his shots the day before**. The following day Mom noted he could not move and he was hospitalized.")(emphasis added); P Ex 15 at 23 ("He is not up-to-date on his immunizations because his mother stopped having them administered after **he developed the transverse myelitis one day following his 4-month immunizations**.")(emphasis added); P Ex 30 at 6 ("Mother reports that he had received his vaccinations, and was cranky and irritable and **the next morning was not moving his legs**. She did contact the primary care physician several times, and one week later, he was admitted to the hospital . . . .")(emphasis added). There is mention of Ethan's TM following vaccination in other records but these entries give no further information regarding the specific time of onset or the course of his condition. These references usually referred to onset shortly after Ethan's four-month vaccinations without specificity. The records from Ethan's hospitalization are at petitioner's Exhibit 10 and contain references to timing that are identical to the records of his neurologist in Exhibit 8.

pediatrician confirms Ethan was well during his visit on December 13, 2005. P Ex 4 at 44. Next, on December 17, Ethan was seen by the pediatrician but the chart note was dictated from memory 24 days later. P Ex 4 at 45. If the description is accurate, it recorded an alert and responsive infant, very decreased motor tone, good reflexes, withdrawal of leg when pinched, and Ethan "**did not have any significant spontaneous movement at all of the lower extremities, would not support weight . . . just still hanging . . . .**" Id. (emphasis added). The pediatrician's contemporaneous note from the December 19 exam reported "a little decreased [muscle] tone," "**does not demonstrate spontaneous movement of his legs**," "significant neurologic change, with loss of spontaneous movement in his lower extremities, **which started the day after he received his immunizations**." P Ex 4 at 44-45 (emphasis added). Both entries consistently report Ethan had no spontaneous movement starting the day after vaccination. As petitioner and her experts point out, the note regarding the December 17 visit was written several weeks later; however, the December 19 pediatrician exam note and a note from the treating neurologist on December 19 of a phone call with the pediatrician provides reinforcement for the information found in the December 17 recollected note. It is significant to note that the physician histories are almost entirely consistent with petitioner's affidavit and the parents' history found in the medical records.

Exhibit 8 contains records from Ethan's treating neurologist who first examined Ethan on December 20. Upon initially seeing the neurologist, Ethan's parent filled out the Patient History Form, noting that Ethan had not "consciously moved his legs in a week after receiving 4 month vaccines." P Ex 8 at 52. Since the pediatrician saw Ethan seven days after vaccination, this corroborates the parents' history of a lack of spontaneous movement beginning the day after vaccination. In his own review of the case, the neurologist observed Ethan was not using his legs after the vaccination, among other symptoms, and that he was "better by day 3." Id. at 53. There is no indication to what "better" refers. His note continued, "seen Sat[urday] – normal [deep tendon reflexes] and sensation, but decreased tone legs [greater than] arms." Id. "Seen this A.M. – little [change], improved a bit. Feeding ok, not sick." Id. "? ADEM or Transv[erse] myelitis? Doubt directly related to imm[unization]?" Id. This record indicates the treating neurologist actually discussed Ethan with the pediatrician on December 19, the day before the neurologist saw Ethan. P Ex 8 at 53 ("spoke with Dr. [] Frostad" . . . "Offered advice consult. – tomorrow . . . "). The undersigned notes that this entry – the notes by the neurologist discussing Ethan's case with the pediatrician by phone on December 19 – is consistent with the recollected notes on Ethan's December 17 pediatrician visit. Compare P Ex 4 at 45; with P Ex 8 at 53. This conversation occurred closer in time to the December 17 visit than the recollected notes created on January 10, 2006. As discussed, the notes of the December 17 visit were called into question by petitioner in particular because they were not dictated on the day of the visit.

Later on, the neurologist explained Ethan's course as the "relatively abrupt onset of diffuse weakness and hypotonia" and following "very closely on the heels of an uncomplicated four-month immunization." Id. at 75. It was also recorded that there was "[w]eakness especially of the lower extremities and irritability **for six days** in a previously healthy four-month-old infant." P Ex 8 at 77 (emphasis added). "He was slightly fussy [on the evening of the vaccinations] . . . The following morning when he woke after an unremarkable night's sleep he was limp and could not move his lower extremities." Id. The neurologist described the nonspecific symptoms that accompanied the limp legs – apathy, lethargy, weak cry and poor

feeding – and stated, "[t]hese symptoms persisted unchanged throughout the day and in to the next two days." He noted improvement as of December 16 but little improvement since that date. Id.

In her Post-Hearing Brief, respondent lists numerous records that place onset of the limp noodle legs the day following vaccination. R Post-Hearing Brief at 20-21. Respondent also points to case law favoring medical records as "trustworthy evidence [as they] contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. at 21 (quoting Cucuras v. Sec'y of the Dept. of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993)).

Third, as presented previously, petitioner offered the expert opinions of Dr. Renfroe and Dr. Byers that the symptoms Ethan suffered during the first three to six days after vaccination were manifestations of his innate immune response to the vaccinations or encephalopathy, and not signs of the autoimmune process that caused his TM. Supra pp. 11-14, 16-21.[32] The presence of an encephalopathy or an exaggerated innate immune response will be discussed specifically. Infra pp. 36-39.

In her testimony, Dr. Byers continually describes all of the symptoms seen in the first three to six days of Ethan's illness as "flu like" symptoms and appears to gloss over the lack of lower extremity movement. Hr'g Tr. at 81-2. She discusses these symptoms as a sign of an innate immune response. It was never explained how "limp noodle" legs and lack of spontaneous movement in the legs is what laypersons know as a "flu-like symptom." Dr. Byers attempted to explain the leg involvement by citation to the collection of VAERS reports. P Ex 31 at 2 (citing P Ex 31-F). As noted previously, the collected reports of hypotonia were not investigated for time of onset. See P Ex 31-F at 4. The article does note that the 54 patients with ataxia, abnormal gait, or both developed symptoms from hours to weeks after vaccination. Id. at 7. Because this study does not investigate these reports specifically regarding time of onset and due to the serious evidentiary limitations of VAERS reports regarding causation, the amount of evidence added to petitioner's case is negligible. Manville v. Sec'y of the Dept. of Health & Human Servs., 63 Fed. Cl. 482 (Fed. Cl. 2004)(upholding a special master's dismissal of VAERS reports because the reports "could be filed by anyone" and did not represent an indication that "the medical community is seeing and reporting a causal relationship."); Analla v. Sec'y of the Dept. of Health & Human Servs., 70 Fed. Cl. 552 (Fed. Cl. 2006)(affirming special master's conclusion that VAERS reports were not sufficient to finding vaccine causation and noting expert testimony that VAERS reports "offer very little information regarding causality."); Nance v. Sec'y of the Dept. of Health & Human Servs., No. 06-730V, 2010 WL 3291896 (Fed. Cl. Spec. Mstr. 2010)(finding petitioner's reliance on VAERS data to be unpersuasive).

[32] The undersigned again notes though that Dr. Renfroe's written reports are unclear on when he believes onset occurred and do not mention Ethan suffering from an encephalopathy. P Ex 20 at 3 (discussing family's report of onset within 24 hours and medical evaluation "4-6 days after"); P Ex 33 (discussing "priming" that may result in a "rapid, acute immune response," evaluation of immune responses as early as 18 hours after exposure, innate immune response and leukocyte recruitment in rats five hours following pertussis exposure, and deferring to Dr. Byers regarding the "rapid onset of Ethan's symptoms").

However, ultimately, Dr. Byers' testimony on this issue rests with Dr. Renfroe as Dr. Byers noted that she was relying upon Dr. Renfroe's opinion regarding the onset of Ethan's TM. Hr'g Tr. at 109-110.

Beyond citing unsubstantiated VAERS reports for this assertion, petitioner provides no support for her experts' opinions that the leg involvement in the first days after vaccination was due to a process other than the one that caused Ethan's TM. Dr. Renfroe admittedly did not know how to interpret the leg involvement and Dr. Byers dismissed it as generalized pain from an innate response. **Critically in this case, Dr. Renfroe concluded that limp legs would be a sign of a spinal cord injury, such as TM, and not a sign of encephalopathy.** Hr'g Tr. at 66-67. Respondent's expert agreed. Supra pp. 22-23; Hr'g Tr. at 125-27, 136-39 ("When you are seeing the marked disparity between function in the arms and the legs you have an internal comparator and absolutely if the legs aren't moving and the arms are moving[,] something bad is happening in between and that means the spinal cord.").

Fourth, respondent offered the opinions of her experts. Dr. Sladky, respondent's expert neurologist, persuasively testified that onset of Ethan's TM began with the prominent leg symptoms observed the day after vaccination. He did not take issue with the parents' description of events and found no reason in the records and affidavit to discount or question the parent's accuracy or reliability. Hr'g Tr. at 158-59. In fact, Dr. Sladky stated the parents' description "was a really eloquent lay-description of acute spinal cord injury." Hr'g Tr. at 125.

Dr. Sladky based his opinion that TM began the day after vaccination upon the medical records, evidencing lack of spontaneous leg movement on December 14. Supra pp. 3-6, 11, 22-24. If there was any true change in spontaneous movement, he attributed it to a phenomenon associated with TM called spinal shock. R Ex A (discussing onset within 24 hours as being implausibly short for an autoimmune response); see Hr'g Tr. 112-62 (discussing 24 hour onset and the phenomenon of spinal shock associated with TM as an explanation for the somewhat variable observations recorded in the first few days following vaccination and onset of paraplegia).

Respondent's Exhibit B-10 discusses the phenomenon of spinal shock and that it is indeed seen in patients with TM. "[M]otor impairment is characterized by weakness, usually flaccid in the initial phase of 'spinal shock', which is severe in two thirds of cases leading to paraplegia; later, flaccid gives place to a spastic paraparesis[33] with tendinous hiperreflexia."[34] R Ex B-10 at 2. This description appears to be congruous with the observations of Ethan's parents, his pediatrician and his treating neurologist. Petitioner did not offer rebuttal evidence or argument concerning spinal shock. Again, most importantly, Dr. Sladky testified that the descriptions in the medical records and petitioner's affidavit were consistent with the process of a spinal injury. Hr'g Tr. at 125.

[33] Spastic is "characterized by spasms" or "hypertrophic, so that the muscles are stiff and the movements awkward" and paresis is the "partial paralysis of the lower limbs." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1766, 1401 (31st ed. 2007).

[34] Hyperreflexia is "dysreflexia characterized by exaggeration of reflexes." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 908 (31st ed. 2007). Dysreflexia is the "disordered response to stimuli . . . ." Id. at 589.

Finally, respondent's expert immunologist was unable to identify or associate Ethan's paraplegia the day following vaccinations as being a consequence of an innate immune response. Hr'g Tr. at 224-26; supra pp. 27.

With this information set forth, the undersigned will now review this evidence in light of the parties' arguments and assertions regarding onset of Ethan's TM. As will be discussed below, the undersigned relies upon respondent's experts that the first sign of Ethan's TM was limp legs observed the day after he received his vaccinations; again, Dr. Renfroe agreed that limp legs were a sign of a spinal cord injury, such as TM, and petitioner advanced no persuasive argument to find the leg symptoms were due to some other process not associated with the TM.

2. Discussion of the above-mentioned evidence and the parties' arguments and interpretations of the evidence

Petitioner contends Ethan suffered a two-stage injury: he suffered the effects of an encephalopathy or an exaggerated innate immune response in the first few days following vaccination and these effects subsided while the adaptive immune response causing TM was beginning approximately six days after vaccination. Petitioner primarily attempts to deal with what is seemingly straightforward evidence found in the medical records by assuming the parents were not reporting Ethan's symptoms accurately to medical professionals and raising doubt regarding the December 17 exam note that was created weeks after the actual exam. Ultimately, the undersigned finds petitioner's attempts to dismiss the medical records unconvincing. Petitioner's arguments and her experts' characterizations of onset often flowed together; the undersigned attempts to parse them out in the discussion below.

a. Evidence of an encephalopathy

The question of whether Ethan suffered from an encephalopathy in the first few days following vaccination amounts to a distraction considering petitioner's own expert neurologist cannot explain how Ethan's symptoms fit into an encephalopathic picture. The contention that Ethan suffered an encephalopathy was first presented in this case by Dr. Byers in her expert report, P Ex 31 at 2; however, Dr. Byers testified that she was relying on Dr. Renfroe that an encephalopathy was present in Ethan. Hr'g Tr. at 81. Dr. Renfroe's written reports do not mention Ethan having an encephalopathy or any reaction other than TM to his vaccinations. In fact, Dr. Renfroe's supplemental report noted his review of Dr. Byers' report but still does not mention an encephalopathy. P Ex 33 (focusing on a discussion of priming the immune system and reasserting the opinion that TM was suffered after vaccination). This opinion from Dr. Renfroe regarding an encephalopathy first appeared at the Hearing. Hr'g Tr. at 12, 33. Encephalopathy was discussed at the Hearing by both Drs. Byers and Renfroe. Petitioner's experts appeared to offer encephalopathy as an explanation for Ethan's condition within 24 hours of vaccination. Notably, the undersigned observes that the treating physicians do not discuss the possibility of an encephalopathy and none of the experts herein discussed Ethan being treated for an encephalopathy in the medical records during or after the first few days of his ordeal.

Referencing petitioner's account of Ethan that is found in the pediatric records, Dr. Renfroe states, "I suspect when [respondent's expert] read this, as when I did, I went 'Oh, my

god. This kid is having a severe and acute reaction to the immunization, an encephalopathy.'" Hr'g Tr. at 33-34. Dr. Renfroe offers encephalopathy during his Hearing testimony based on the parents' description of Ethan on the days following vaccination. Hr'g Tr. at 33-43. He relies on the non-specific symptoms identified in the very medical records he dismisses as unreliable. From those same records, he dismisses the parents' early reports of limp legs.[35] Beyond the non-specific symptoms, Dr. Renfroe points to no other cognitive or neurological changes that would evidence an encephalopathy. Dr. Renfroe specifically admitted the leg symptoms would not be a sign of an encephalopathy. Hr'g Tr. at 66.

As pointed out by the undersigned, Dr. Renfroe relies on the parents' description as it would pertain to an encephalopathy but dismisses their description as it would pertain to a spinal cord injury. This inconsistent reliance was poorly explained and the undersigned notes that Dr. Renfroe was admittedly unable to identify the "limp noodle" legs as a symptom of an encephalopathy. Hr'g Tr. at 65-66. Dr. Renfroe urges the court to dismiss the parents' focus on leg problems because they, or specifically the mother according to Dr. Renfroe, were frightened and unable to account for Ethan's symptoms properly. Hr'g Tr. at 36-38. Dr. Renfroe's use of the medical records in this fashion was very unpersuasive.

During the Hearing, the undersigned noted to Dr. Renfroe that he had never heard of an acute encephalopathy presenting with paraplegia such as was seen in Ethan. Hr'g Tr. at 65. Dr. Renfroe responded, "**I'm not saying that either**. I'm saying that I've got a kid and what scares me [is] that this child is – 'couldn't cry. Makes quiet, pathetic moaning sounds.' That this is a sick child." Hr'g Tr. at 66 (emphasis added). Further, when asked about the leg symptoms, Dr. Renfroe stated, "[i]n my view – I don't know what to do with this as I've said." Hr'g Tr. at 66. And Dr. Renfroe again cites the parents' distress as why they focused, apparently wrongly, on problems with Ethan's legs. Hr'g Tr. at 66; Hr'g Tr. at 67 ("[W]hen we see – when a Momma provides us a wonderful history – I can imagine this young lady who is scared to death."); Hr'g Tr. at 70 ("She focuses on the legs, I'm concerned, retrospectively."). Dr. Renfroe admitted that limp legs would be a sign of a spinal cord lesion, as seen in TM, and he stated that limp legs would not be a sign of an encephalopathy. Hr'g Tr. at 66-67.

Throughout his testimony, there was no reasonable response from Dr. Renfroe as to why the physician's observations of limp legs on December 19 was to be credited while the parents' written history, the petitioner's affidavit, the in-office history given on December 19 and the non-contemporaneous physician note from the December 17 exam were to be dismissed. Even this list disregards the numerous patient histories recorded while Ethan was being treated in December 2005 and January 2006 that note onset of leg symptoms the day following vaccination. Supra pp. 32 n. 30, 32-33. Dr. Renfroe assumed one or both of the parents were frightened about Ethan's condition, not reporting correctly and that petitioner was applying the later event of paraplegia to her history of the days before December 19.

[35] Likewise, Dr. Byers dismissed the parents' description of leg symptoms as well by asserting Ethan was generally unwell, did not want to stand due to painful muscles, and this was noted by the parents as "wet noodle" legs. Hr'g Tr. at 109; supra pp. 19-20.

It is understandable that a parent could report medical histories with some inconsistencies given the disconcerting events happening to their child. However, there is simply nothing in the record that would suggest that either parent was so distraught over Ethan's condition that they were confused or unable to report information the physicians needed for diagnosis and treatment. The medical records almost consistently document onset of paraplegia the day after vaccination.[36] For his determination of onset, Dr. Renfroe inexplicably relies on the first physician's exam noting the paraplegia that was contemporaneously written on December 19; however, he ignores the fact that this same record also gives a history of limp legs starting the day after vaccination, December 14. Dr. Renfroe ultimately admitted that he did not know when Ethan's TM symptoms began, greatly injuring the persuasive value of his opinion. Hr'g Tr. at 35. Most significantly, Dr. Renfroe later admitted that he could not say when the first sign or symptoms of Ethan's TM began. Hr'g Tr. at 35.

Respondent persuasively undercut petitioner's claim of an encephalopathy. An encephalopathy is defined as "any degenerative disease of the brain." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 622 (31st ed. 2007). The Act itself defines an encephalopathy for purposes of Table injuries; Ethan's symptoms in the first few days following vaccination do not fit this description of an encephalopathy. Qualifications and aids to interpretation, 42 C.F.R. § 100.3(b)(2)(discussing significant changes in consciousness or mental state indicative of an encephalopathy). Regarding the proposition that Ethan suffered from an encephalopathy following vaccination, Dr. Sladky acknowledged that the generic symptoms Ethan suffered, such as crankiness and lethargy, might accompany an encephalopathy. Hr'g Tr. at 128. However, he noted Ethan lacked other features more specific to an encephalopathy, "I don't hear any evidence of a defused disorder of consciousness, an inability to respond to his environment." Hr'g Tr. at 128. "[T]he evolution of the symptoms was entirely consistent with an acute myelopathy . . . ." Id. When questioned about this during cross-examination, Dr. Sladky stressed that an encephalopathy went beyond simply a child feeling poorly. Hr'g Tr. at 138-39. Whereas petitioner's experts must dismiss and qualify the events recorded in Ethan's medical records, respondent's expert neurologist finds no reason to doubt the medical records and further finds the process Ethan suffered as recorded in the medical records wholly consistent with the progression of TM.

The medical literature provided by both parties discusses non-specific symptoms often seen initially with TM. See, e.g., P Ex 38 at 5, John H. Menkes, et al., CHILD NEUROLOGY 587 (7th ed. 2006)("Before the onset of acute loss of spinal cord function, there are often nonspecific symptoms such as nausea, muscle aches, and fever. . . . The neurological picture is most frequently characterized by the presence of back pain and pain in the lower extremities, gait disturbance due to weakness, paraplegia, and parasthesias."); R Ex B-12 at 3, F.S. Pidcock, et al., Acute transverse myelitis in childhood, Center-based analysis of 47 cases, 68 NEUROLOGY 1474 (2007)(describing pain present at onset in 75% of the cases studied, weakness in 89%, sensory loss or numbness in 91%); R Ex B-10 at 2 (discussing how some "patients report unspecific complaints, as fever or myalgias, before onset"). However, petitioner's expert immunologist, Dr. Byers, also presented literature that such non-specific symptoms, excluding Ethan's leg

[36] See, e.g., P Ex 4 at 46 (noting onset on December 13, 2005, which was the date of immunization). This record actually notes onset of leg symptoms on the day of vaccination, a timing sequence that makes relation to the vaccinations more improbable.

symptoms, could be associated with the innate immune response to vaccination. P Ex 43 at 2, PHYSICIANS' DESK REFERENCE 1385 (1998); P Ex 31-F. Dr. Byers, however, did not address the opinions or medical literature that these non-specific symptoms are also associated with the onset of TM. For neurological issues, Dr. Byers deferred to Dr. Renfroe. Dr. Renfroe did not rebut Dr. Sladky's testimony on this issue.

Regardless of the etiology of these non-specific or flu-like symptoms, it is the lack of spontaneous leg movement that is unambiguous and this symptom is not explained by petitioner's reference to an innate immune response to vaccination. Both of the expert neurologists testified the lack of spontaneous leg movement would be evidence of a spinal cord injury. Moreover, Dr. Rose, respondent's expert immunologist, was unable to see how the leg symptoms were a manifestation of a normal innate immune system response to vaccination. Dr. Byers attempted to contradict this, attributing the leg symptoms to general pain or another process of the innate immune system based upon unsubstantiated VAERS reports, but her efforts were unpersuasive.

The petitioner has not presented persuasive evidence that Ethan suffered from an encephalopathy starting the day of or the day after vaccination and leading up to the point when petitioner contends Ethan's TM began. Petitioner's own experts cannot point to anything in the medical record indicative of an encephalopathy beyond the nonspecific, flu-like symptoms, which could evidence any number of illnesses or injuries including TM. It must be emphasized that Dr. Sladky testified that all of Ethan's symptoms suffered within a day of his vaccinations were entirely consistent with the process of TM. It also cannot be overemphasized that the limp legs are not a symptom of encephalopathy, but are a symptom of a spinal cord injury. Based on the medical records, the admissions by petitioner's expert neurologist, and respondent's expert opinions, the undersigned finds no evidence of Ethan suffering an acute encephalopathy.

b. Evidence of an exaggerated innate immune response

During the hearing, Dr. Byers characterized the hypothesized encephalopathy alternatively as an exaggerated innate immune response to the vaccinations. Hr'g Tr. at 99-100; supra pp. 13-14. However, respondent's expert immunologist specifically noted, "[t]he fact that Ethan did not have an adverse response to infections and has previously received vaccines with no problems suggests further that he has no inherited genetic impairment in controlling innate immunity." R Ex B at 4. Like an encephalopathy, an exaggerated immune response is not mentioned in the medical records or observed by the opposing experts. Supra pp. 14-15; R Ex B at 4. It is not noted in his medical records that Ethan presented with other unusual immune responses to previous infections or vaccinations. Petitioner's characterization does not appear consistent with the medical records or the other experts' view of the symptoms. Further, the exaggerated innate immune response does not explain hypotonia and lack of spontaneous movement in the legs. This argument appears to be highly speculative as it was not developed and, besides Dr. Byers' words, there is little support or reasoning for it.

c. Dr. Renfroe's reliance on a physician's contemporaneously-written exam note to find onset and timing

Changing focus slightly, petitioner relies upon her expert, Dr. Renfroe, for his opinion that Ethan's TM began six days after vaccination. Six days after vaccination, December 19, 2005, was the point Ethan was objectively examined by his pediatrician and there was a contemporaneous exam note created recording the leg symptoms. Hr'g Tr. at 12; P Post-Hearing Brief at 31-32. This is the point at which Dr. Renfroe opined the TM began. Ultimately, however, Dr. Renfroe admitted that he could not say when the first sign or symptoms of Ethan's TM began, only that it was observed by a medical professional six days later. Hr'g Tr. at 35. In her Post-Hearing Brief though, petitioner focused on this time frame for the beginning of Ethan's TM.

Given the quantity of information contained in petitioner's affidavit and the medical records, it is unreasonable to dismiss all of this evidence and accept only the contemporaneously-recorded pediatric exam note on December 19 as the first symptom of Ethan's TM. Petitioner has offered no compelling reason why the undersigned should dismiss the numerous references in the medical records and petitioner's affidavit, especially when the December 19 exam note also recounts onset of paraplegia the day after vaccination. P Ex 4 at 44 ("He received his 4-month-old immunizations six days ago, since that time he has just not been himself – this is documented well by parents' history that they bring in. Their main concern is that he has had minimal spontaneous movement of his legs since that time . . . .").

Onset of an alleged injury is often discussed regarding the Act's statute of limitations and there is no support in the case law that the date of onset of an injury is the first, contemporaneously documented physician examination. See Cloer v. Sec'y of the Dept. of Health & Human Servs., 654 F.3d 1322, 1339-40 (Fed. Cir. 2011)(holding onset for the purpose of the statute of limitations occurs with the first symptom or manifestation of an injury regardless of petitioner's knowledge of the condition); Wilkerson v. Sec'y of the Dept. of Health & Human Servs., 593 F.3d 1343 (Fed. Cir. 2010)(relying on the observation of a layperson for the first sign of the injury and deciding the statute of limitations runs from the first symptom of the condition in hindsight, not from when that symptom is recognized as a symptom of the condition); Markovich v. Sec'y of the Dept. of Health & Human Servs., 477 F.3d 1353, 1357 (Fed. Cir. 2007)(rejecting petitioner's argument that eye blinking was a too subtle or ambiguous symptom to constitute onset of the alleged injury).

Upon review of the evidence herein, the undersigned finds that the symptoms suffered by Ethan – observed by his parents within 24 hours of vaccination and reported to treating doctors throughout Ethan's treatment – were evidence of the onset of his TM. Petitioner's experts never approached persuasiveness with their disregard of Ethan's leg symptoms occurring the day after immunization, which Dr. Renfroe agreed is a symptom of a spinal cord injury, or their attempts to attribute the leg symptoms to another biological process.

d. Conclusion regarding onset of Ethan's TM

Reviewing the totality of the record, the undersigned finds no compelling reason to doubt the accuracy of the medical records and the parents' recorded observations, and no compelling reason to accept petitioner's characterizations of the events in the records. Petitioner failed to rebut respondent's assertion that Ethan suffered spinal shock, which is associated with TM,

supported by medical literature and explains the changes seen in Ethan's legs. The parties' expert neurologists agree "limp noodle" legs are a sign of a spinal cord injury and not of an encephalopathy. Petitioner was further unable to support Dr. Byers' argument that Ethan suffered a dysregulated innate immune response that caused the symptoms seen in the first few days after vaccination, including the leg symptoms. The great weight of evidence, which is fairly consistent from different portions of the medical records, shows the onset of TM – the lack of spontaneous movement of Ethan's legs – was first observed the day after vaccination when Ethan awoke on December 14, 2005. Accordingly, Ethan's TM began on December 14, 2005.

C. MEDICAL THEORY CAUSALLY CONNECTING VACCINATION AND THE INJURY

The first prong of Althen requires preponderant evidence of a "medical theory causally connecting the vaccination and the injury." This requirement has been referred to as the "can cause" prong: can the vaccine cause the alleged injury. Pafford v. Sec'y of the Dept. of Health & Human Servs., No. 01-165V, 2004 WL 1717359 (Fed. Cl. Spec. Mstr. 2004), aff'd 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). The undersigned views the first prong of Althen as inquiring whether the vaccines in question could cause the alleged injury, akin to general causation. Pafford v. Sec'y of the Dept. of Health & Human Servs., 451 F.3d 1352, 1354-56 (Fed. Cir. 2006)(noting the special master applied the tests of Althen and Shyface correctly and discussing the "can cause" aspect of the first prong and the "did cause" aspect of the second prong); see also Veryzer v. Sec'y of the Dept. of Health & Human Servs., 100 Fed. Cl. 344, 352-53 (Fed. Cl. 2011)(explaining the first two prongs of Althen in terms of general causation, prong one, and specific causation, prong two).

To meet the first prong of Althen, petitioner "must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly, 592 F.3d at 1322 (citing Knudsen, 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also Broekelschen, 618 F.3d 1339, 1345 (Fed. Cir. 2010). Petitioner's proof cannot merely establish a "plausible" or "possible" causal link between the vaccine and the injury; the proof must meet the statutory standard of preponderance. Moberly, 592 F.3d at 1322; see also Caves, 100 Fed. Cl. at 132, 144, aff'd per curiam No. 2011-5108, slip op. (Fed. Cir. Feb. 14, 2012).[37]

[37] Notably, in her Post-Hearing Brief, petitioner continually characterizes her burden under this prong of Althen as merely a "plausible" theory and presenting a binary choice that the standard under Prong I is either an unsupported but plausible medical theory or a scientifically-confirmed theory. P Post-Hearing Brief at 24-25. However, beyond supplying this incorrect and oversimplified "either/or" construct, petitioner fails to acknowledge the Federal Circuit's language in Moberly, which was issued one year and seven months prior to the filing of petitioner's Post-Hearing Brief and involved the same law firm as represents petitioner herein. Indeed, a petitioner is not required to show causation by a standard of scientifically certainty. However, a special master may "require some indicia of reliability to support" an expert's theory of causation in a case. Moberly, 592 F.3d at 1324; see also Moberly, 592 F.3d at 1322 ("While petitioner's acknowledge that the statute requires proof of causation by a preponderance of the evidence, . . . they appear to be arguing for a more relaxed standard. They repeatedly characterize the test as whether Molly's condition was 'likely caused' by the DPT vaccine. By that formulation, however, they appear to mean not proof of causation by the traditional "more likely than not" standard, but something closer to proof of a 'plausible' or 'possible' causal link . . ., which is not the statutory standard."). The undersigned notes this is not the first time this law firm has argued mere biologic plausibility after the Federal Circuit's decision in Moberly and then failed address this language. "[A]ny reasonable argument in favor of 'biologic plausibility' would need to address

Regarding fulfillment of Althen prong I, petitioner argued she provided a plausible medical theory through Dr. Renfroe's opinion that "the DTaP vaccine has 'been shown to have been associated with [TM]." P Post-Hearing Brief at 26, filed Aug. 22, 2011. The undersigned notes that Dr. Renfroe's statement only alleges an association, not a casual relationship. Petitioner further pointed to Dr. Renfroe's use of the Fenichel text, noting "[t]he belief is widely held by many specialties [sic] that a prior infectious illness or immunization causes [TM] . . . in children." Id. (citing P Ex 20-A at 264). Petitioner conveniently left out Fenichel's next statement, "[n]o evidence supports this belief." P Ex 20-A at 264. Petitioner also referenced Dr. Renfroe's reliance on a Mayo Clinic web page, which states "TM may be caused by vaccinations . . . ." P Post-Hearing Brief at 26 (citing P Ex 20-B). Again, petitioner somewhat mischaracterized the information in this exhibit. The web page reads, "[r]arely, [TM] may develop following certain vaccinations, including those for chickenpox and rabies. It is unclear how [TM] and vaccinations are related." P Ex 20-B at 3. Ethan did not receive the chickenpox or rabies vaccinations and the webpage does not make any affirmative statement regarding vaccinations **causing** TM or vaccines other than chickenpox and rabies being associated with TM.

Petitioner cited case reports submitted by Dr. Renfroe to meet her burden of proof. P Post-Hearing Brief at 26 (citing P Ex 20-C and P Ex 27). Dr. Renfroe admitted case reports alone cannot evidence a causal connection. Hr'g Tr. at 44. Dr. Sladky, respondent's expert, criticized use of these case reports as they are anecdotal evidence and they do "not rise to that level of credibility and fail to substantiate the contention" that the vaccine was the cause. R Ex A at 4. Another piece of petitioner's own evidence, the Kerr article, also cautions reliance on case reports; "such case reports [of vaccine-induced autoimmunity] must be viewed with caution, as it is entirely possible that two events occurred in close proximity by chance alone." P Ex 39 at 3.

Case reports have been discussed frequently in this Program. Although providing some circumstantial evidence regarding causation, the limitations of case reports have also been noted. See Campbell v. Sec'y of the Dept. of Health & Human Servs., 90 Fed. Cl. 369 (Fed. Cl. 2009)(noting validity in the special master's observations regarding the limited evidentiary value of case reports); see also Shepperson v. Sec'y of the Dept. of Health & Human Servs., No. 05-1064, 2008 WL 2156748 (Fed. Cl. Spec. Mstr. 2008)(noting a single case report is not "sufficiently probative to begin the evidentiary climb to a preponderance."); Caves v. Sec'y of the Dept. of Health & Human Servs., No. 07-443, 2010 WL 5557542 (Fed. Cl. Spec. Mstr. 2010)(discussing the limited role of case reports), aff'd, 100 Fed. Cl. 119 (Fed. Cl. Jun. 24, 2011); aff'd, No. 2011-5108, slip op. (Fed. Cir. Feb. 14, 2012)(per curiam).

Beyond the case reports, petitioner also cites numerous cases in which compensation was awarded for vaccines allegedly causing TM. P Post-Hearing Brief at 24, n. 9. As one may imagine, it is difficult to compare individual cases within the Program with any certainty without

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Moberly." Davis v. Sec'y of the Dept. of Health & Human Servs., No. 07-451V, 2012 WL 1357501 (Fed. Cl. Spec. Mstr. 2012)(finding the attorney's failure to cite or discuss Moberly, upon which entitlement to compensation was denied, in a Motion for Review was grounds for reduction of attorney fees), appeal docketed, No. 07-451V (Fed. Cl. Apr. 19, 2012).

examining the specific factual underpinnings of each case. The undersigned does point out that, by petitioner's own parentheticals provided in the footnote of her brief, the cases she cites involve vaccines Ethan did not receive. Ethan did not receive vaccinations for MMR, hepatitis B or influenza on December 13, 2005. However, petitioner did cite one case awarding compensation based on a vaccine Ethan did receive and a brief case search exhibits other cases in which petitioners were compensated for TM and received one or more vaccines that Ethan received. P Post-Hearing Brief at 24-25 (citing Herkert v. Sec'y of the Dept. of Health & Human Servs., No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr. 2000); see also Doe/53 v. Sec'y of the Dept. of Health & Human Servs., No. [redacted]V, 2009 WL 5605698 (Fed. Cl. Spec. Mstr. 2009)(awarding compensation on a Vaccine Act claim alleging TM following tetanus diphtheria, MMR and Hep B vaccinations); Hargrove v. Sec'y of the Dept. of Health & Human Servs., No. 05-694V, 2009 WL 1220986 (Fed. Cl. Spec. Mstr. 2009)(finding entitlement to compensation on a Vaccine Act claim alleging TM following DTaP and other vaccinations); Ortegren v. Sec'y of the Dept. of Health & Human Servs., No. 10-247V, 2011 WL 5291561 (Fed. Cl. Spec. Mstr. 2011)(awarding compensation on a Vaccine Act claim alleging TM following DTaP, Hep B, IPV, PCV and rotavirus vaccinations).

In her Post-Hearing Brief, petitioner points to the theory of molecular mimicry for her evidence related to Althen prong I and notes that "respondent's expert neurologist . . . agreed that TM is a disease that can be caused by molecular mimicry. P Post-Hearing Brief at 27 (citing Hr'g Tr. at 148). However, the question petitioner fails to address is whether a **vaccine** can cause TM through molecular mimicry. It is true that petitioner here has supplied a medical theory; what she arguably has not provided is a medical theory "causally connecting the vaccination and the injury." Althen, 418 F.3d at 1278; Moberly, 592 F.3d at 1322 ("A petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probably, not medically or scientifically certain.'")(citing Knudsen, 35 F.3d at 548-49); Moberly, 592 F.3d at 1324 ("[petitioners' expert] conceded that there was no evidence in the record suggesting that the proposed mechanism was **at work in [petitioner's] case**.")(emphasis added); Pafford, 451 F.3d at 1356 (affirming the special master's analysis requiring petitioner to show the vaccination "actually caused the alleged symptoms in her **particular** case.")(emphasis added); Caves v. Sec'y of the Dept. of Health & Human Servs., 100 Fed. Cl. 119, 128-30 (Fed. Cl. 2011)(distinguishing between a general theory of molecular mimicry causing TM and the specific assertion of vaccination causing TM via molecular mimicry), aff'd, No. 2011-5108, slip op. (Feb. 14, 2012)(per curiam).

In my long history deciding cases since the inception of this Program, demyelinating injuries are frequently claimed and litigated. These cases are filled with complex medical evidence and involve theories of causation, such as molecular mimicry, that are not entirely understood by doctors and medical researchers at present. The scientific reality is that well-credentialed experts sometimes can and do disagree regarding whether vaccinations can induce injuries through molecular mimicry. In this case *sub judice*, the undersigned finds it unnecessary to determine whether petitioner has shown a medical theory by preponderant evidence in light of the timing element discussed below. Because of the complexity of vaccine-related autoimmunity and the fact that deciding this prong is unnecessary to the outcome of this case, this Decision presumes petitioner met her burden in that respect while acknowledging the great amount of

speculation, argument and doubt from medical practitioners and researchers that there is in fact a causal relationship between vaccinations and TM.

D. A LOGICAL SEQUENCE OF CAUSE AND EFFECT SHOWING THAT THE VACCINATION WAS THE REASON FOR THE INJURY

The second prong of Althen requires preponderant evidence of a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." This prong is sometimes referred to as the "did cause" test: in petitioner's case, did the vaccine cause the alleged injury. Pafford v. Sec'y of the Dept. of Health & Human Servs., No. 01-165V, 2004 WL 1717359 (Fed. Cl. Spec. Mstr. 2004); see also Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010)("Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case…"); Moberly, 592 F.3d at 1324-26. Petitioner must show that the vaccine was the "but for" cause, or in other words, "the vaccine was the 'reason for the injury.'" Pafford v. Sec'y of the Dept. of Health & Human Servs., 451 F.3d 1352, 1356 (Fed. Cir. 2006). This is akin to actual or specific causation.

Petitioner argues that she has exhibited a logical sequence of cause and effect in that Ethan was healthy, he received vaccinations, he experienced TM within days of vaccination, and no other cause was identified for his TM. E.g., P Post-Hearing Brief, 27-30, filed Aug. 22, 2011; P Reply to Respondent's Post-Hearing Brief, 9-12, filed Nov. 21, 2011.[38] In her Post-Hearing Brief, petitioner notes the treating physicians' reference to Ethan's vaccinations when discussing his condition as evidence of a logical sequence of vaccine cause and effect. P Post-Hearing Brief at 28-30. Petitioner clings to speculative notes from Ethan's treating neurologist, which may only be historical or contextual references. Id. at 30. As discussed above, the treating physicians did not identify Ethan's vaccinations as causative of his TM. When the subject of vaccine-causation was brought up relating to Ethan's future vaccinations, the treating neurologist expressed his view that there was no connection and the temporal association was merely coincidental. Supra at pp. 6-7. Petitioner fails to acknowledge the treating physicians were only noting a bare temporal proximity. Moberly, 592 F.3d at 1323 (affirming the special master's and the Court of Federal Claims' conclusion that the medical records did not contain support for petitioner's causation theory even though treating physicians noted temporal proximity).

Regardless, the onset of Ethan's TM within one day of receiving the vaccinations is an implausibly short time frame as testified to by both sides. It is specifically this time frame that makes the sequence of events illogical for vaccine causation. Thus, an in depth discussion under Prong II is omitted.

E. AN APPROPRIATE TEMPORAL RELATIONSHIP GIVEN ONSET OF TM WAS WITHIN 24 HOURS OF VACCINATION

[38] The undersigned notes this section in the Reply to Respondent's Post-Hearing Brief is almost identical, if not completely identical, to the section of petitioner's own Post-Hearing Brief. Compare P Post-Hearing Brief, 27-30, filed Aug. 22, 2011; with P Reply to Respondent's Post-Hearing Brief, 9-12, filed Nov. 21, 2011. In fact, several sections of the Reply brief are indistinguishable from sections of the initial Post-Hearing Brief. This redundancy is not a reply to respondent in her Post-Hearing Brief, adds nothing of substance to the case and will be taken into consideration when petitioner applies for attorneys' fees and costs for this case.

The third prong of Althen is "showing of a proximate temporal relationship between the vaccination and injury." In de Bazan v. Sec'y of the Dept. of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008), the Federal Circuit explained that "the proximate temporal relationship prong requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." Id. (citing Pafford, 451 F.3d 1352, 1358; Althen, 418 F.3d at 1281). "Merely showing that injury occurred after administration of a vaccine is insufficient." Veryzer, 100 Fed. Cl. at 356.

It is in the third prongs of Althen where petitioner's case clearly fails. While a petitioner may be able to show a literal temporal association, the petitioner herein is unable to show a medically-accepted temporal relationship between the vaccination and the alleged injury given the evidence and testimony submitted by both sides. Pafford, 451 F.3d at 1358; see also de Bazan, 539 F.3d at 1352; Veryzer, No. 06-522V, 2011 WL 1935813, *23-24 (finding petitioner had not established a medically appropriate time frame between vaccination and onset of injury), aff'd, 100 Fed. Cl. 344, 356 (Fed. Cl. 2011), appeal docketed, No. 12-5034 (Fed. Cir. Jan. 3, 2012). Because the undersigned finds onset of TM occurred within 24 hours of vaccination, the temporal relationship is not medically appropriate as testified to by all of the experts. Evidence offered by petitioner herself forecloses the possibility that Ethan's development of TM within 24 hours was vaccine-related.

All of the experts, to varying depths, discussed what must transpire before inflammation and demyelination cause observable motor dysfunction. P Ex 33; P Ex 31; R Ex B; see also supra pp. 19-26. This evidence and evidence offered in other cases shows a complex cascade of events that must occur prior to the onset of an adaptive, autoimmune response becoming measurable by laboratory diagnostics, plus several more steps before the injury actually presents in observable symptoms. See also Contreras, 2012 WL 1441315, *9-12 (Fed. Cl. Spec. Mstr. Apr. 5, 2012)(discussing in-depth the multiple steps needed for a neurological injury caused by molecular mimicry, offered by experts for both petitioner and respondent), appeal docketed, No. 05-626V (Fed. Cl. May 4, 2012).

Dr. Sladky, respondent's expert neurologist, offered medical literature from the IOM discussing the hypothetical time frame, a minimum of five days, in which development of a demyelinating injury from vaccine might occur. Supra p. 11. Further, the case reports cited by Dr. Renfroe in support of vaccine-causation all evidence a temporal association between TM and vaccinations that was longer than 24 hours, ranging between 6 days and 21 days after vaccination. Supra pp. 9-10.

Dr. Byers, petitioner's expert immunologist, offered testimony that onset within 24 hours of vaccination would not support vaccine causation in this case. Hr'g Tr. at 108. Dr. Byers also testified that onset of TM within seventy-two hours of vaccination would also not be an appropriate time frame. Hr'g Tr. at 101-02. Dr. Rose, respondent's expert immunologist, testified that the beginning of an adaptive immune response – not the outwardly observable symptoms of the neurological injury – would not be seen until at least 96 hours after vaccination when the person had previously encountered the antigen, such as with a second booster vaccine.

Supra pp. 14-16, 25-26. Dr. Byers appeared to agree with this testimony from Dr. Rose. Hr'g Tr. at 101 ("It takes four to seven days for the vaccination to result in activation of the adaptive immune system resulting in an autoimmune disease.").

Given the evidence presented by both parties, 24 hours is unequivocally too short of a time period for TM to present if the vaccinations were to blame. The undersigned found Ethan's TM began within 24 hours after immunization. Supra p. 40-41. Thus, petitioner is unable to show onset of Ethan's TM was within a medically appropriate time frame under Althen prong III.

F. AN APPROPRIATE TEMPORAL RELATIONSHIP IF ONSET OF ETHAN'S TM WAS SIX DAYS AFTER VACCINATION

Even accepting Dr. Renfroe's belief that onset of TM was six days post-vaccination – when Ethan was examined by the pediatrician and the exam note was contemporaneously made – respondent provided further evidence that onset of TM symptoms six days after vaccination is not a medically appropriate time frame to be vaccine-related. Supra pp. 25-26. Relying on the testimony of Dr. Rose, respondent notes that at least ninety-six hours is necessary for a measurable immune response, evidence of antibodies. R Post-Hearing Brief at 30 (citing Hr'g Tr. at 182-89, 212-15). Thereafter, it would take additional time for the antibodies to proliferate and cause the lesion on the spinal cord, thus manifesting clinical symptoms, perhaps as much as four days given the injury discussed, perhaps longer. Hr'g Tr. at 188-215. Regarding the testimony by the experts at Hearing on the appropriate timing, it was not always clear whether the measured event was the adaptive immune response or the manifestation of symptoms of that adaptive immune response. The concepts of an "immune response" and "development of clinical symptoms" were often used interchangeably even though petitioner's experts did not argue with the description of the steps that must occur for molecular mimicry to cause TM. Notably however, the IOM report discussed by respondent's expert neurologist finds, "the earliest clinical evidence of neurological dysfunction in these animal models emerges around seven days, with the majority in the range of ten to fourteen days." R A-5 at 4. Based on these findings, the IOM hypothesized a latency time frame between five days and six weeks. Id. This five day period appears to conflict with Dr. Rose's estimate of nearly eight days as a rapid appearance of clinical symptoms from an adaptive immune response attacking one's own body.

The issue – how much time it takes to develop symptoms of an autoimmune demyelinating injury – has been examined frequently in the Program. E.g., Contreras, 2012 WL 1441315 (denying compensation because a one-day onset of TM following vaccination is insufficient to show causation), appeal docketed, No. 05-626V (Fed. Cl. May 4, 2012); Veryzer, 2001 WL 1935813, *23-24 (finding onset of demyelination or toxicity within hours of receiving a vaccination not medically appropriate), aff'd, 100 Fed. Cl. 244 (Fed. Cl. 2011), appeal docketed, No. 2012-5034 (Fed. Cir. Jan. 3, 2012). It is likely to continue to be a critical issue as many demyelinating injuries are alleged under the Act. As in this present case, care is not always taken by the parties or experts to differentiate between onset of the autoimmune response and onset of symptoms of the injury in discussing the medically appropriate time of injury onset. Review of the expert evidence in this case and discussions in other cases demonstrates the issue of an appropriate time frame for actual symptoms to appear deserves careful attention to

distinguishing between what Dr. Rose says are two different time frames – the time necessary for a measurable adaptive immune response in the body and the time required to manifest clinical symptoms when that adaptive immune response causes injury in the body.

Considering preponderant evidence in this case shows the onset of TM symptoms within 24 hours of vaccination and petitioner's experts' concession that 24 hours is not a medically appropriate time frame, it makes sense to leave further discussion of this timing issue in autoimmune, demyelinating cases for another, more appropriate case.

VII. CONCLUSION

Because she is unable to show TM began within a medically appropriate time frame, petitioner is unable to provide preponderant evidence that the vaccinations in this case caused her son's TM. Petitioner's claim is denied. The Clerk of the Court is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Gary J. Golkiewicz
Gary J. Golkiewicz
Special Master